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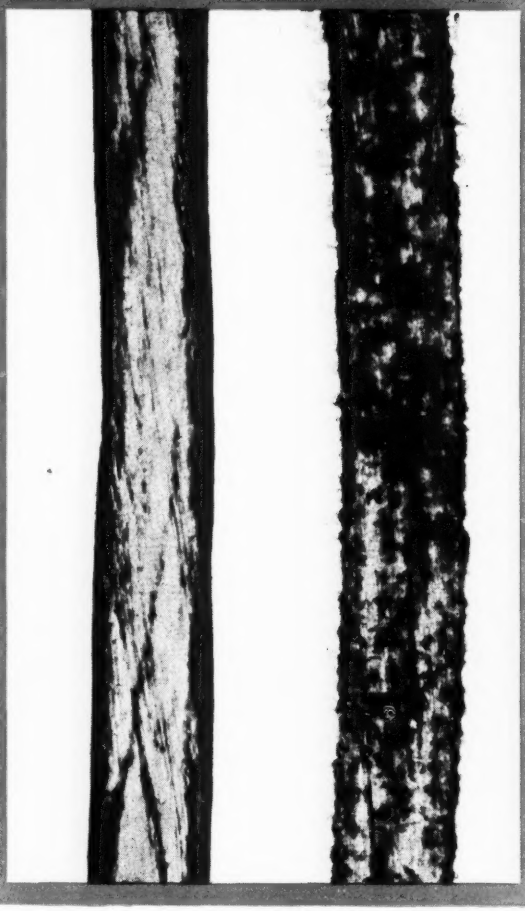
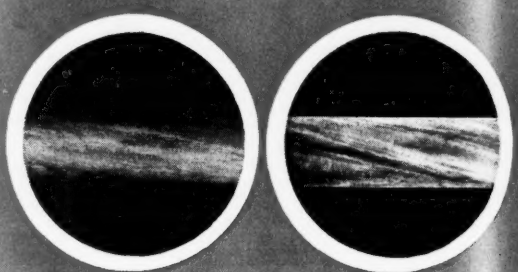


Photomicrography shows why **D & G** gut is stronger— more flexible



D & G gut

Photomicrograph* shows smooth surface of D & G SURGICAL GUT with no fraying or roughness. The soft matte finish prevents knots from slipping. No grinding to size. Full natural strength is preserved.

Another leading gut

Photomicrograph* detects surface fraying and roughness. This gut was ground to size. It appears uniform to the naked eye, but the powerful camera lens shows imperfections which may cause weakness when a knot is tied.

*Medium chromic gut, 5-0; light field method; 106 x

D & G gut

Photomicrograph** shows firm, even cohesion of plies—twisted into strands before chromicizing —for greater flexibility. Natural collagen firmly bonds the plies —holds the twist. This results in greater knot strength under stress.

Another leading gut

Photomicrograph** detects separate plies in this gut. Here each ply was chromicized before twisting into suture strand. This process limits natural bonding —lowers flexibility and tensile strength — encourages fraying.

**Medium chromic gut, 00; dark field method; 27 x

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Photomicrography shows what the hand cannot feel

Photomicrographs (unretouched) by E. J. Thomas, Stamford Laboratory, Research Division of American Cyanamid Company, Stamford, Connecticut.

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THE CONSIDERATION OF SOME PROBLEMS OF LARGE BOWEL CARCINOMA

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THE SURGERY OF MALIGNANT DISEASE of the colon has advanced greatly since Plummer was playing an important part in the diagnosis of cancer of the colon and Judd was actively engaged in their eradication. They are among the commonest of the malignant lesions of man. They rank high in this country among the causes of death from malignant disease each year. They are frequently engrafted upon the only relatively common hereditary precancerous lesion now known in man—the adenomatous polyp—especially as it relates to the condition known as diffuse adenomatous polyposis of the large gut.

And yet, in spite of all we increasingly know about the malignant lesions of the colon and rectum and their varying symptomatology, frequently a considerable lag exists in the general acceptance of the methods best calculated to diagnose these lesions and the therapy which will most frequently provide long survival. There is still far too often a long period of delay in diagnosis. The philosophy of care, once the diagnosis has been made, has not as yet received general acceptance. The time may well come when our successors may conclude that much of our thinking in this field has been superficial.

Many of the areas in which it is reasonable to assume that general acceptance should have been achieved are still controversial. Some frown upon certain of the surgical procedures that are being carried out, while others continue them, not because they have been shown to provide longer survival, if even as long as other procedures, but because they may provide a lower immediate mortality and a more normal anatomic end result.

Conditional recovery from an operation is under no circumstances synonymous with prolonged survival. Much of what is being published today may indeed be open to serious question. It would be a simpler matter to make accurate and significant deductions from the data obtained from hospital records if the biostatistician played an important part in organizing the clinical investigation which was to be carried out. Such data would perhaps be acceptable to all clinicians rather than to the author and his associates and those with a similar viewpoint.

Abridgement of the Judd-Plummer Memorial Lecture, Rochester, Minnesota, October 28, 1955.
From the Department of Surgery and the Harrison Department of Surgical Research, Schools of Medicine, University of Pennsylvania, Philadelphia.

To be sure, over the last half century, we have witnessed a slowly changing concept of the surgical care of these patients. During the first 30 years the operations frequently were not only limited as regards the amount of large bowel resected, but even more limited in regard to the amount of adjacent mesentery removed. In nearly every instance, resections of the right, transverse, and left colon, sigmoid, and rectum were done in stages. For lesions of the right side of the colon, it was more or less the accepted practice to anastomose the terminal ileum to the transverse colon and to resect the right colon at another operation. Modifications of the Bloch-Mickulicz operation also were devised for the eventual resection of these lesions. A review of the literature of that period is not germane to our subject, for it is replete with reports of the successful removal of the tumor and a reduction in the operative mortality. It must be frankly admitted, however, that there was no generally accepted method for recording mortality during this period of surgical history. The extent of a so-called radical excision varied as greatly as did the procedure which was given this name.

Recently, Lewis Lasagna, in a paper entitled, "The Controlled Clinical Trial" makes this statement: "The clinician who would avoid nihilistic rejection or trusting acceptance of all such claims, or capricious decisions as to their merits, is well advised to adopt a yard-stick, a set of criteria, that will improve his chances of making sound evaluations." While Lasagna's remarks were not directed toward the efforts of the surgeons, they apply equally well to their efforts. He goes on to say, "on the one hand, fundamental principles will be accented, not only to provide a framework for subsequent discussions, but to distinguish clearly between the important primary considerations and less essential embellishments and refinements of technique." Surgeons might well heed this admonition.

The recent studies on morbidity from cancer in the United States, published in *Public Health Monograph No. 29*, show cancer of the large bowel and rectum rank as the No. 1 cancer in man. The data reported in that document show that in the large bowel the incidence of cancer among females exceeds that among males by a little less than 10 per cent. While in general the sex differential of cancer incidence for specific sites is much the same for both whites and negroes, cancer of the rectum is an exception to this statement. In the white population, the incidence rate for males is higher than that for females, while, in the negro population, the situation is reversed, the rate being slightly higher among females than the rate for males. While the incidence rate for cancer of the upper gastrointestinal system is higher in the negro than in the white, this circumstance is reversed for the lower part of the alimentary tract, the intestines and rectum, where the respective rates are 46 for whites and 29 for nonwhites. The excess morbidity among whites comes from the fact that the incidence of cancer of the large intestines in the white group is nearly twice as great as that among the negro group, the former having an incidence of 27 per 100,000 compared to an incidence of 15 per 100,000 in the latter group. One can easily determine from the data provided in the monograph that, in age adjusted cancer incidence rates for specific sites, the incidence of cancer of the large intestine and rectum combined is greater than that of any other cancer studied. This makes the problem all the more important.

No one would now doubt that cancer of the large bowel, including the rectum, is among the commonest of the major cancers afflicting mankind. No one would doubt but that the majority of these lesions can be diagnosed early, and that 75 per cent of them are found within the first 26 centimeters of the anus. Gradual realignment has occurred in our thinking that a great many of the cancers of the large bowel are engrafted upon adenomatous polyps. There seems to be hardly any question but that nearly all of the multiple primary malignant lesions are engrafted upon adenomatous polyps. It is becoming more generally accepted by clinicians that

diffuse adenomatous polyposis is a hereditary precancerous lesion. It should be constantly kept in mind that there is, according to Duke, no essential difference in the biologic difference between the congenital hereditary type of diffuse polyposis and the nonhereditary (solitary as Duke calls it) type of diffuse polyposis. They both eventually and inevitably give rise to cancer. Furthermore, the incidence of carcinoma in the polyposis occurring in long standing ulcerative colitis is higher than is generally believed. In these patients, 10 per cent or more develop cancer 5 years or more after the polyposis develops. At present there is little chance for long survival of a patient with a cancer of the colon or rectum short of adequate surgery, even when the variations in the biologic behavior of all malignant tumors are considered.

Whose responsibility is it constantly to point these matters out until these concepts are generally accepted? While surgery may prove in the future not to be the optimal therapy, it is at the present time the only satisfactory therapy which is available. Certainly, no one should now question the fact that the patient has much to gain by a thorough operation and very little to lose. Recent improvements in preoperative preparation and postoperative care, together with a complete change from our earlier thinking of the operative procedures best calculated to provide for long survival, if the patient recovers from the operation, now offer real safeguards.

In many areas considerable difference of opinion still exists regarding the care of these lesions. There are areas in which more or less unanimity of opinion could be obtained, and others in which generalization in one direction or another is still too diffuse. I should like to define some of these areas in order to determine whether or not more or less general agreement can be reached to the end that the period of disability associated with operation be shortened, and survival following operation be lengthened. These were goals to which Starr Judd and Henry Plummer were devoted.

There are certain aspects of surgical therapy upon which general acceptance would now be highly desirable. The one relates to the circumstance that only in the presence of acute obstruction is a two stage operation necessary, and under these circumstances the first stage of the operation should consist of a proximal colostomy. The colostomy should be so placed that it provides for the achievement of a clean and an empty bowel. These criteria are not achieved when a cecostomy is done. At times a cecostomy is an operation of necessity, but it should not be an operation of election. In the absence of acute obstruction, the judicious use of the Miller-Abbott tube, or a tube achieving similar results, makes it possible in nearly every instance to resect the bowel and restore continuity in a single stage.

Another matter concerns itself with the extent of the resection. An adequate resection of the bowel and the widest possible resection of the adjacent mesentery is at present the procedure best calculated to provide for long survival. If the bowel is adequately prepared prior to operation, the extent of the resection of the bowel and its contiguous mesentery need only be limited by the determination prior to resection of the adequacy of the remaining blood supply. There is ample evidence in the literature that many variations from the descriptions of blood supply as given in the commonly used textbooks of anatomy exist. The right and middle colic arteries are branches of the superior mesenteric artery and supply the ascending colon, the hepatic flexure, and the transverse colon. The left colon and the upper rectum are supplied by the left colic and the sigmoidal arteries which are branches of the inferior mesenteric artery. The superior mesenteric artery may be double, and the inferior mesenteric artery may occasionally be absent. Under these circumstances the, entire intestinal tract is supplied by the superior mesenteric artery. At times, there is a failure of anastomosis between the left and the middle colic arteries. At times, the right colic artery is absent, and at others the middle colic artery may not be present. Occasionally, the middle colic and the left

colic arteries fail to anastomose. The important thing to remember from these many inconsistencies of the normal arterial arrangement is that resection and anastomosis should be done at a point at which the remaining bowel receives an adequate blood supply. Only under these circumstances, can one be satisfied that the integrity of the anastomosis will be secured. The surgeon must determine at operation the adequacy of the blood supply before resection is done.

Too many resections of the colon are being done which are too limited in extent, too limited to assure the longest possible survival subsequent to operation. Also, many of the resections of the adjacent mesentery are even more limited in extent. This frequently occurs because the surgeon believes that a more limited resection of the mesentery will provide greater insurance from vascular difficulties subsequent to resection. It may be better to extend the area of resection of bowel and mesentery from the standpoint of both securing the anastomotic site and achieving prolonged survival.

For lesions of the right side of the colon, we should have general acceptance of the fact that the entire right colon, hepatic flexure, and a considerable portion of the proximal transverse colon be resected, and that the mesentery be freed by dissection and excised along the posterior abdominal wall until the descending duodenum is reached. Retroperitonealization of the posterior wall need not be attempted and is, in fact, impossible if the dissection has been as complete as it should be.

Whether gut continuity is re-established by end-to-end suture of the ileum to transverse colon, or by end-to-side, or side-to-side, probably makes very little difference, but it would seem to be preferable to do an end-to-end anastomosis whenever this is possible. If this precept is accepted, end-to-end suture will be done in nearly every instance.

In the transverse colon, the perversity of the lymph node spread is such that limited resections of the transverse colon are just as undesirable from the standpoint of prolonged survival as in any other area of the colon. Here too, at times, considerable uneasiness exists regarding the security of the suture line because of certain variations in blood supply.

One need only to be reminded that the surgeon can achieve wide resection of the bowel and adjacent lymph bearing areas and, in addition, protection of the suture line if the entire transverse colon is removed and the hepatic flexure anastomosed to the descending colon, or if necessary to the upper sigmoid. Some surgeons will consider that this is too extensive a resection, that it often results in diarrhea in patients, and that after all it is probably unnecessary. I find myself less concerned with minor inconveniences to the patient and more concerned by the problem of long survival, if not cure. If the patient is frankly told of the alternatives, experience has convinced me that the patient, knowing that an operation has been necessary, will happily accommodate himself to the operation which offers him a better chance for future well-being.

In carcinoma of the hepatic flexure, there has long been acceptance of the fact that it is better to resect the entire right colon and the proximal half of the transverse colon and the contiguous mesenteries. This has not been true for splenic flexure carcinoma, in spite of the fact that the end results of splenic flexure carcinomas have not been as good as we might expect them to be. In this area, not only should the bowel resection and the contiguous mesentery be widely resected, but the spleen and its mesentery should be excised much more frequently than is now being done. It is far simpler and much more sound to resect the left half of the transverse colon, the splenic flexure, the spleen, and part or all of the descending colon and their contiguous mesenteries, and anastomose the midtransverse colon to the remaining distal bowel than to do a limited resection. This is likewise true for the lesions involving the descending colon. Time and again, the surgeon must remind himself that the patient, in agreeing to any operative

procedure, places the responsibility on him to eradicate, if possible, not only the primary disease but also areas of possible extension of the malignant process. If this is constantly kept in mind and thoroughly heeded, limited resections will rapidly become obsolete.

In the sigmoid colon, a thoroughly adequate resection of the bowel and widespread resection of the sigmoid mesentery are again not only desirable but mandatory. The inferior mesenteric artery should be located to determine its presence, and if the surgeon is satisfied that adequate arterial circulation can be maintained, the inferior mesenteric artery should be ligated adjacent to its origin and not in the lower reaches of the left lower quadrant. The mesentery concerned with this general area of the bowel should be excised together with the contained lymph nodes. It is in the extent of the resection, both of the bowel and the mesentery, that we should take a fresh look. The anastomosis of the bowel for the restoration of gut continuity differs in nowise from that done with a more limited resection.

There are instances in which low anterior resection may be done, but I am convinced that when the surgeon is attempting cure, the indications for low anterior resection become fewer and fewer. The patient is, of course, immediately elated that he has not been left with an abdominal colostomy, but this is not a matter which should seriously concern anyone who is contemplating cure of the patient. I have all too frequently felt this deep satisfaction of the patient in the early period after operation, only later to have a troubled conscience in the belief that a more radical operation might have provided longer survival when recurrence took place.

I have repeatedly stated that operations of the "pull-through" type for carcinoma of the rectum were devised to cater to the whims of a distraught patient, rather than being based on sound reasoning. There are those who state that ample justification will be found in studies of lymph node spread in an upward, downward, or lateral direction. I am not convinced by these studies, for they deny, in part at least, certain of our basic concepts of spread of malignant disease.

Finally, a perineal anus is an abomination while a controlled abdominal colostomy is compatible with normal living once the patient adjusts to its presence.

If the patient is properly prepared prior to operation and if acute obstruction is not present, an extensive operation can and should be done in a single stage. In the great majority of instances, it can be done without the aid of anastomosing clamps. It is, however, of really great importance, I believe, to clamp the bowel proximally and distally in order to prevent seeding of carcinomatous cells as described by Warren Cole.

Whenever possible, it is desirable that the anastomosis be done as an open anastomosis without the use of clamps. There will be less trouble with suture lines when this method is more generally adopted. The so-called aseptic operations fall far short of being an adequate answer to the most careful preparation prior to resection.

In the geriatric patient, the tendency to get into difficulty at the suture line from a variety of postoperative conditions is greater than in the younger group. For this reason, I frequently use the Witzel operation and insert a rubber catheter of modest size into the colon well proximal to the anastomosis which provides a vent for the escape of gas and liquid. I have never regretted placing it in the gut, and at times have regretted not doing so.

If it is accepted that 100 per cent of the patients with carcinoma of the colon will have died in a few years if nothing is done, and a very considerable number of them will have a long period of survival, or even cure, if a really radical procedure is undertaken, the mandate of the surgeon is clear and unequivocal. Surgeons must search themselves that the motives which lead them to do lesser operations for a disease which will kill 54,000 or more of our people this

year are not conditioned by an initial lower mortality, or an immediately grateful patient. The surgeon should do those procedures best calculated to get the patients well and keep them well.

Lewis Mumford, in his volume, *The Condition of Man*, said, "One must not merely feel for the suffering of other men, but like the physician, know what is good for them even if that knowledge leads to a remedy so drastic that it involves the physician no less than the patient."

It is to be hoped that before many more years pass chemotherapy will have made possible the cure of many of the common malignant lesions without resort to widespread resections of bowel and mesentery. Perhaps when such agents become available we shall know more of the biologic factors that condition malignant disease in certain organs, and we may then extend therapy to the prevention of these lesions which with the passing of each year take too high a toll in human lives.

Until that time—which internist and surgeon so hopefully await—comes, early diagnosis and early adequate therapy, in most instances, will give the patient the best chance of prolonged survival if not cure. DePeyster and Gilchrist have recently summarized the necessities of an adequate procedure for cure as "(1) to prevent manipulative venous spread; (2) to prevent implantation; (3) to excise sufficient bowel to include maximum intramural spread; and (4) to remove the cancer by en bloc excision with the dependent echelons of lymph node spread." These reasonable suggestions will, I hope, find wider acceptance than they have in the past, for just so long as no more adequate concept of therapy is available they offer the patient the only chance of cure.

BLOOD VOLUME CHANGES IN CASES OF CEREBRAL TRAUMA AS DETERMINED BY RADIOACTIVE ISOTOPES

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THAT ALTERATIONS in the chemical constituents of the blood occur following cerebral trauma had been known since the time of Claude Bernard. However, only recently, since the advent of increased knowledge about, and improved methods of, determining alterations, have the electrolyte changes in neurosurgical states been the subject of attention.

Less interest, however, has been placed on the hematologic alterations associated with head injury. Mardomingo noted alteration in the red blood cell count in 46.1 per cent of 53 cases studied. The work of Rosenow, Houssay and associates, and Hoff particularly suggested that alterations in the composition of the blood appear on central stimulation. This work was carried out on experimental animals, and the effect of central stimulation on the white blood cell elements particularly was studied. In a comprehensive paper, Lucia has summarized the relationship of the central nervous system to hematopoiesis.

For several years we had been impressed by the striking clinical picture of secondary anemia which was observed in many patients suffering closed head injury (10). Hematologic studies of such cases demonstrated, in many instances, a profound anemia as manifested by low levels in the red blood cell, hemoglobin, and hematocrit determinations. The mechanism of the anemia mentioned above has to date remained unexplained.

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This study was performed under A.E.C. contract AT (11-1)-215.

It seemed likely that acute changes in whole blood volume in cases of concussion might be a factor in the development of this anemia. Since no such studies appeared available, it was decided to study the blood volume in a series of patients who had suffered craniocerebral trauma. The results of this study and the problems encountered are the subject of this report.

MATERIALS

We selected only those cases of closed head injury in which cerebral trauma was the sole factor in producing the clinical picture. Cases of cerebral trauma associated with shock, fractures of long bones, visceral injury, or extensive lacerations causing blood loss were excluded.

Twenty-one such patients were studied in detail. Each patient had an admission blood volume determination with hemoglobin and hematocrit studies. These studies were repeated at 24 hour intervals for varying periods of time, depending on the patient's clinical course.

TECHNIQUE

The study of this type of patient raised several technical difficulties. First, such patients are usually admitted to the hospital at the most inopportune times (usually in the late hours of the evening or early hours of the morning). Secondly, the conventional dye techniques, such as the Evans blue method, were unsatisfactory because of their inherent objections, namely, the discoloration of the patient, the time required in the determination, and the fact that daily determinations of value could not be easily done.

TABLE I.

Patient Age, yrs. Sex	Injury	Admission Pulse	Admission Blood pressure	X-ray findings	Admission blood volume studies Normal	Admission blood volume studies Measured	Admission blood volume studies Per cent deviation	Admission hemogram RBC	Admission hemogram Hgb. gms.	Admission hemogram HCT	Result
A.O. 14 mo. M	Fell 5 feet striking head on concrete walk	112	110/64	Simple skull fracture	1242	1019	−19	4.0	11	37	Recovered
C.J. 53 F	Auto accident	128	138/82	No fracture	3799	5730	+51	3.9	10	38	Recovered
C.F. 37 F	Fell 5 feet striking head on concrete floor	72	120/80	No fracture	3509	3487	− 1	3.7	11.8	36	Recovered
M.M. 7 M	Auto accident	118	130/90	No fracture	1863	2600	+39	3.2	9.8	28	Recovered
H.A. 38 M	Auto accident	96	140/80	Simple skull fracture	4968	5800	+16	3.5	10.7	35	Recovered
R.B. 38 M	Beaten about the head by an assailant	88	132/94	No fracture	3795	4370	+15	3.6	10.5	37	Recovered
M.S. 8 M	Auto accident	112	108/70	No fracture	1587	2190	+38	3.7	10	34	Recovered
R.R. 6 M	Fell 6 feet striking head on concrete walk	120	80/50	Simple skull fracture	1863	2970	+58	3.8	8.4	32	Recovered
P.L. 20 F	Auto accident	108	150/80	No fracture	3349	4270	+27	3.8	11.0	39	Recovered
C.D. 46 M	Auto accident	118	100/60	Simple skull fracture	7108	6970	− 2	4.1	13	41	Recovered
J.F. 18 M	Motorcycle accident	124	118/94	No fracture	4692	5750	+22		15	48	Recovered
D.S. 38 M	Struck on head by flying railway mailbag	88	150/95	No fracture	5175	5125	0		14	46	Recovered
E.B. 18 M	Auto accident	68	120/65	No fracture	4416	5125	+16		11.3	43	Died
M.T. 50 M	Fell from moving truck	60	158/100	No fracture	7176	5250	−27		13.9	54	Died
A.H. 70 M	Fell 6 feet striking head on concrete drive	110	140/90	No fracture	5326	4350	−19		11.9	56	Died
L.H. 8 M	Struck on head by falling steel bar	114	114/40	Simple skull fracture	1746	1604	− 9	3.6	10	34	Recovered

TABLE I.

Patient Age, yrs. Sex	Injury	Admission Pulse	Admission Blood pressure	X-ray findings	Admission blood volume studies Normal	Measured	Per cent deviation	Admission hemogram RBC	Hgb. gms.	HCT	Result
N.R. 8 F	Struck by auto	160	80/40	No fracture	1610	1260	−22	3.1	10	32	Recovered
J.W. 6 M	Fell from bicycle striking head	96	100/60	No fracture	1725	1680	− 3		13	40	Recovered
W.F. 7 M	Fell from slide striking head on concrete	100	102/80	No fracture	1725	1440	−17		11.7	40	Recovered
A.H. 6 M	Fell 8 feet striking head on concrete	104	100/80	No fracture	1587	2200	+38	3.6	9.4	36	Recovered
R.P. 9 M	Struck on head by steel pipe	96	140/80	No fracture	2487	3430	+37	3.3	10	38	Recovered

The carbon monoxide technique was not, in our opinion, applicable to the severely injured patient.

However, the determination of blood volume utilizing radioactive isotopes seemed ideal for this study. A thorough study of the radioactive isotopes available was made to determine the most applicable and convenient one for this project.

The isotopes used to measure total blood volume are radioactive iron, phosphorus when used in particular form, and chromium. All of these isotopes can be incorporated in one manner or another within the red cell itself. Iron was unsatisfactory because of the difficulty of tagging the erythrocytes with this isotope. The phosphorus isotope was not used because the phosphorus turnover is so rapid, in that the determinations of blood volume must be done within one-half hour after injection if accurate measurements are to be obtained.

The work of Gray and Sterling with radioactive chromium indicated that this would be an ideal tracer element. However, since this was a clinical research project, dealing with acute emergency patients, it was desired to obtain whole blood volume determinations in the acutely injured patient immediately upon admission. Hence, a method of tagging a universal donor (Rh negative type O) blood which could be held ready for immediate use was developed.

Approximately 95 per cent of the hexivalent ions of radioactive chromium become attached to the red cells. By this technique, if kept refrigerated, very little hemolysis occurred over a period of 3 to 4 weeks. The great advantage of the radioactive chromium tagged cells was that the material was always available and necessitated only 1 injection into the patient but permitted determination of the blood volume over a period of several days. Control studies on normal individuals indicated this to be a workable plan. As the series enlarged, certain bizarre results were sporadically observed. On some patients accurate blood volumes could be obtained from a single injection over a period of 4 or 5 days, while on others it was impossible to obtain reliable results after 24 to 36 hours. In every instance in which the results appeared unreliable the blood volume seemed to increase rapidly which showed that tagged cells were being removed from the vascular system at a much higher rate than normal. This seems to be in direct variance with the common belief that Rh negative type O blood is truly a "universal donor" type. It would in-

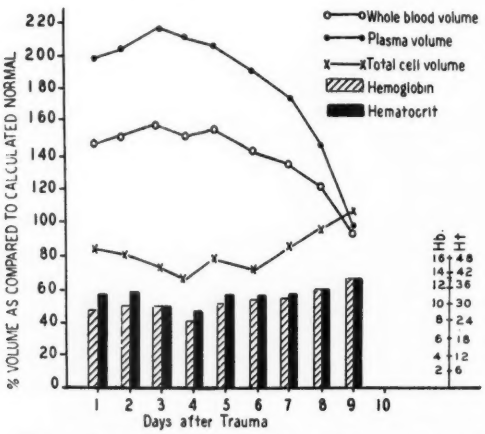

FIG. 1. Patient C. J. (tracer, IHSA). This curve shows an expanded whole blood and plasma volume immediately following injury. Note that the hemoglobin and hematocrit values were lowest on the fourth day which coincided with the time of maximal plasma volume increase and of lowest total cell volume.

dicate that the life in the vascular system of these foreign cells, in some patients, was relatively short.

Because of these difficulties some patients were studied by using radioactive iodinated human serum albumin as a tracer element. Such studies gave data of the total blood volume as well as a direct measurement of plasma volume.

A new well-type scintillation counter having a sensitivity almost 1,000 times more than our previous counters was developed for use in these blood volume determinations.

The radioactive sources used for injection were prepared and stored in sterile rubber stoppered containers. Each such ampule contained a 10 cubic centimeter volume of solution which had approximately 20 millicuries of radioactivity. All sources were measured for their activity in the well-type scintillation counter prior to use. In each instance a standard solution that contained a similar amount of radioactivity as the source to be injected was identified and retained for use in later calculations.

The solution for injection was aspirated from the ampule into a sterile syringe and then injected into an antecubital vein of the patient. Following the injection a volume of tap water equal in amount to the volume given was aspirated into the syringe and then reinjected into the original container.

Fifteen minutes were allowed for adequate mixing of the radioactive substance within the patient's circulation. At the end of this time a sample of blood was obtained by venipuncture from the opposite arm to the site of injection. All blood samples were collected in dry heparinized tubes. The calculation of blood volumes was made after redetermining the radioactive content in the standard solution, and the residual activity in the wash water. The difference between these values represented the actual amount of radioactive material given the patient. The radioactivity of carefully measured amounts of the heparinized blood samples was determined.

Knowing the total amount of radioactivity injected and the concentration of activity in a carefully measured volume of blood allowed easy calculation of the total blood volume on the basis of dilution.

A report covering this new counter and counting technique is in preparation.

RESULTS

Twenty-one patients with craniocerebral injury had blood volume and hemogram determinations on hospital admission and at 24 hour intervals following trauma. The results of these determinations were compared to the accepted normal levels as calculated for the sex and average body weight of the patient. Table I summarizes these findings. The ages ranged from 14 months to 70 years. There were 16 males and 5 females.

In 17 patients (80 per cent), there was a significant deviation of the blood volume from the accepted normal levels on admission to the hospital. In 11 patients of this group, the blood volumes were increased above normal; in 6 patients, the blood volumes were less than the normal. In 4 patients there was no significant alteration of admission blood volume from the range of calculated normal for the patient.

Of the 17 patients showing these initial variations, three basic patterns of volumetric changes were observed by serial study during the period following injury.

In one group (11 patients) there was an initial increase in blood volume followed by a gradual return of the whole blood volume to normal. The per cent of increase in total blood volume ranged from 15 to 58 per cent above the calculated normal. The rate of return of blood volume to normal levels was variable, but in general paralleled the patient's clinical improvement. Figures 1 and 2 are illustrative cases of this type. These graphs chart the percentage of variation from the calculated normal for the patient.

Figure 1 represents the volumetric studies using iodinated human serum albumin of patient G. J. This 53 year old female was injured in an automobile collision. On admission to the hospital she was unconscious. There was a profound pallor of the skin and conjunctiva. The blood pressure was 138/80. The pulse rate was 128 per minute. There were bilateral periorbital ecchymoses. The neurologic examination was noncontributory. The roentgenograms were negative for fracture of the skull.

The patient remained unconscious for 5 days following injury. She was discharged from the hospital 12 days after admission, alert and oriented.

Figure 2 charts the result of the blood volume studies of patient M. M., using iodinated human serum albumin as a tracer element. This 7 year old boy was admitted to the hospital immediately after being struck by an automobile. Except for the unconscious state the neurologic examination was normal. The blood pressure on admission was 130/90. The pulse rate was 118 per minute. The child was pale. There were multiple contusions about the scalp, trunk, and extremities. Roentgenograms showed no evidence of fracture. This child regained consciousness 12 hours after injury. He was discharged in 6 days completely recovered.

A second group (6 patients) had a less than normal blood volume on admission to the hospital. The percentage of decrease ranged from 9 to 27 per cent. Four of these patients survived. Two of this group had a subsequent expansion of the blood volume to levels well above the normal. Figure 3 is an example of such a response.

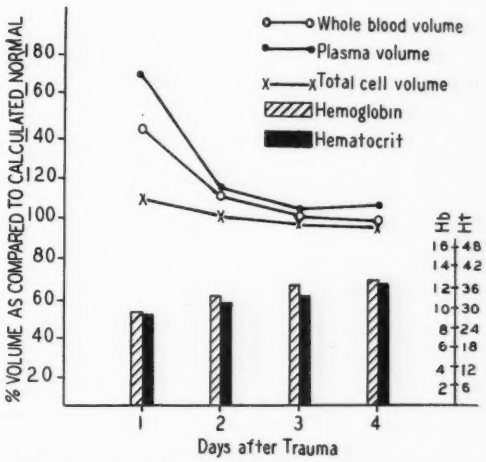

FIG. 2. Patient M. M. (tracer, IHSA). An immediate expansion of the plasma volume, following injury, was associated with a marked anemia. The hemoglobin and hematocrit values increased as the blood volumes returned to normal levels.

This graph records the daily blood volume determination of patient N. R. using radioactive chromium tagged red cells. This 8 year old girl was struck by an automobile about 30 minutes prior to admission to the hospital. She was unconscious. There was a small left supraorbital laceration. The admission blood pressure was 80/40. The pulse rate was 160 per minute. There was repeated vomiting. The pupils were dilated but reacted to light. The remaining neurologic examination was noncontributory. One hour following injury the child had a generalized convulsion lasting 3 minutes. Roentgenograms of the skull revealed no evidence of fracture.

Immediately following admission the patient was given 200 cubic centimeters of whole blood intravenously. She remained unconscious for 72 hours following injury. On the fifth hospital day she was given an additional whole blood transfusion of 200

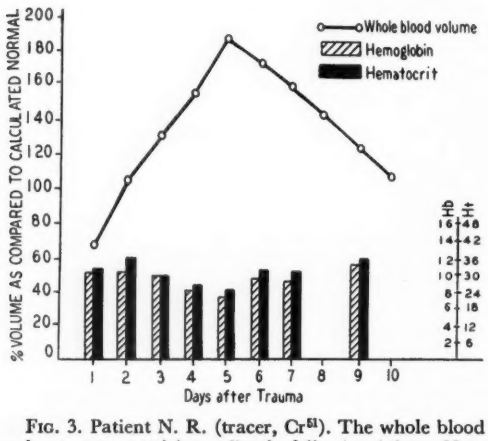

FIG. 3. Patient N. R. (tracer, Cr^{51}). The whole blood volume contracted immediately following injury. Note the progressive expansion of blood volume paralleled by an increasingly severe anemia. Both of these alterations were at their maximum on the fifth day after injury. This patient was given 200 cubic centimeters of whole blood on the first and fifth hospital day.

cubic centimeters. The subsequent clinical course was one of improvement. She was discharged from the hospital, walking, 12 days after injury.

Serial studies of the 2 remaining patients in this group showed that the initial contraction of the blood volume was followed by an increased volume, but not significantly above the calculated normal value for

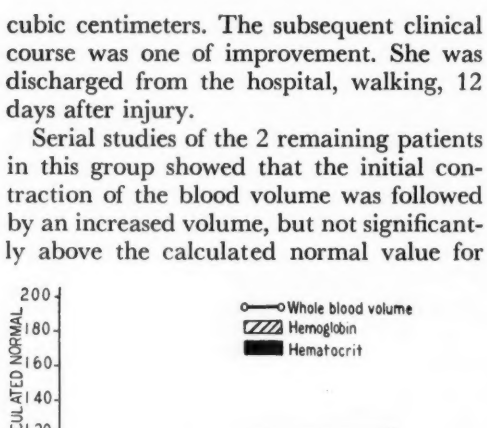

FIG. 4. Patient J. W. (tracer, Cr^{51}). Note the curve shows an initial contraction of whole blood volume. This is followed by a limited expansion to levels only slightly above the normal. There was no significant alteration in the hemogram.

that patient. Figure 4 represents the serial changes in such a patient using radioactive chromium tagged red cells as a tracer element. This patient, J. W., was a 6 year old boy who fell from his bicycle and struck his head on a concrete sidewalk. He was admitted to the hospital unconscious. There was a contusion of the forehead. The blood pressure was 100/60. The pulse rate was 96 per minute. The neurologic examination, except for unconsciousness, was normal. About 2 hours after admission the child responded to noci stimuli, and 6 hours after injury he was completely conscious. The roentgenograms showed no fracture. He was discharged 5 days after injury in excellent condition.

A third group of patients showed no volumetric change in the period following injury of more than a plus or minus 5 per cent of the calculated normal volume. Figure 5 represents volumetric studies using iodinated human serum albumin in such a patient. This patient, C. F., was a 37 year old female who fell from a foot stool on which she was standing, striking her head on a concrete floor. She was admitted to the hospital unconscious. There were several bouts of vomiting immediately following admission. There was a right periorbital ecchymosis. The blood pressure was 120/80. The pulse rate was 72 per minute. The neurologic examination was otherwise noncontributory. Two hours after injury the patient was completely conscious. She was discharged on the fifth day after injury without any neurologic deficit.

Twelve of the 21 patients had an anemia on admission. In 8 of this group the anemia became more profound and progressive in the days immediately following trauma. As the clinical course improved, with or without transfusion, the anemia disappeared and the hemogram adjusted to normal levels.

Of the 12 patients with anemia 9 had an increased blood volume (Fig. 6). In every one of these cases in which the plasma volume was directly measured it was increased. In 5 of these 9 patients, there was also a less

than normal total cell volume. In these cases, the actual loss of erythrocytes and the plasma dilution combined to produce the anemia. These studies do not explain the mechanism of anemia in those 3 cases which were not accompanied by an increase in whole blood volume.

So far we have concerned ourselves with the volumetric data per se. We were, however, interested to see whether or not some correlation existed between the clinical picture of the patient and the volumetric curves.

In order to obtain some clinical yardstick of comparison, we decided to employ the period of unconsciousness as an index of the degree of intensity of the injury. We arbitrarily classified those cases as "severe" (concussion) in which the period of unconsciousness was greater than 24 hours, at least, and in some instances longer than several days. We considered a "moderate" injury (concussion) those cases in which the period of unconsciousness varied from less than 24 hours to a few minutes, in most instances less than 6 hours. In general, it may be stated that all patients with severe (concussion) injury showed a progressive blood volume increase and an increasingly severe anemia in the immediate days following injury. Those patients with a moderate (concussion) injury initially had a quantitively less marked volumetric change on admission determinations, and only rarely showed any progression in the intensity of volume change or in the degree of anemia during the period following trauma. Indeed, in some instances in this group there was a constriction of the whole blood volume and no evident anemia.

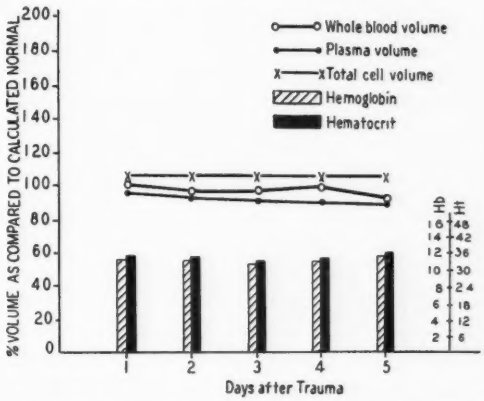

FIG. 5. Patient C. F. (tracer, IHSA). No significant change from the normal of either the blood volume or hemogram values.

DISCUSSION

The cases reported here show acute changes in the whole blood volume in patients sustaining craniocerebral injury. In over 80 per cent of the cases there was a sudden expansion, or constriction, of the blood volume following injury. In over one-half (57 per cent) of the total cases there also developed an acute anemia. These alterations may be precipitated by vasomotor changes resulting from central nervous system injury.

That head injury could result in circulatory failure had been reported by Denny-Brown and Russell. They described vasoconstriction with moderate injuries and vasodilatation occurring with severe cerebral injury. These workers described the pathophysiology as a vagoglossopharyngeal stimulation which counteracted the pressor effect to the vasomotor center.

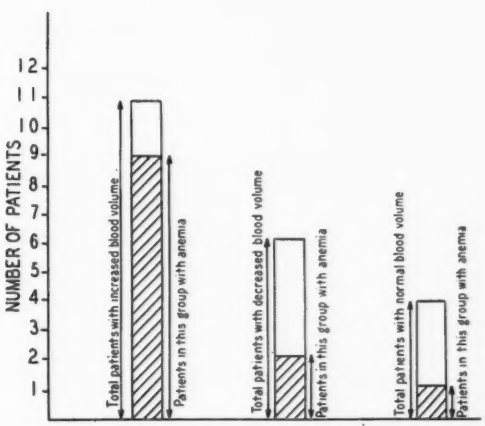
NUMBER OF PATIENTS
Total patients with increased blood volume
Patients in this group with anemia
Total patients with decreased blood volume
Patients in this group with anemia
Total patients with normal blood volume
Patients in this group with anemia

FIG. 6. Distribution of patients with anemia as related to the whole blood volume changes.

Gurdjian and Webster concluded from their experimental studies on head injury that vasocirculatory failure was due to paralysis of the vasoconstrictor center with resultant vasodilatation.

The expansion of the intravascular space that may result from the vasodilatation demands an increase in whole blood volume in order to maintain adequate circulatory dynamics. Since there are no known large reservoirs of red blood cells, the rapid (compensatory) increase in the volume must come in the plasma compartment. No large plasma reserves are known in man. Acute increases in blood volume may be at the expense of the extracellular fluid. This transfer of fluid into the vascular compartment would be enhanced by a lowered intracapillary pressure (vasodilatation). This would result in a dilution of the cellular elements, producing a lowered hemoglobin and hematocrit, consistent with the development of an acute anemia.

In some of the patients with moderate concussion there was a constriction of the blood volume and in some no evident anemia. In these cases it is conjectured that vasoconstriction rather than vasodilatation was the physiologic effect of injury.

CONCLUSION

1. Blood volume studies were made on 21 patients with craniocerebral injury utilizing radioactive iodinated human serum albumin and chromium tagged red blood cells.

2. Seventeen patients (80 per cent) had an alteration in blood volume from the calculated normal.

3. Eleven patients (52 per cent) had an initial increase in blood volume.

4. Six patients (28 per cent) had an initial constriction of blood volume.

5. Generally, expansion of the plasma volume occurred in those cases in which the cerebral trauma was of a more severe degree.

REFERENCES

1. Bernard, C. Influence de la section des pedoncules ceribelleux moyens sur la composition de l'urine. C. rend. Soc. biol., 1849, 1: 14.
2. Denny-Brown, D., and Russell, W. R. Experimental cerebral concussion. Brain, Lond., 1941, 64: 93.
3. Gray, S. J., and Sterling, K. Tagging of red cells and plasma proteins with radioactive chromium. J. Clin. Invest., 1950, 29: 1604–1613.
4. Gurdjian, E. S., and Webster, J. E. Experimental and clinical studies on the mechanism of head injury. Proc. Ass. Res. Nerv. Ment. Dis., 1945, 24: 48.
5. Hoff, F. Klinische Beitraege zur Frage der zentralnervoesen Regulation des Blutes. Klin. Wschr., 1932, 11: 1751.
6. Houssay, B. A., Royer, M., and Orias, O. Hémoglobine et nombre d'erythrocytes des chiens hypophysoprives. C. rend. Soc. biol., 1931, 108: 496.
7. Lucia, S. P., and Marasse, H. F. The central nervous system and hematopoiesis. J. Nerv. Ment. Dis., 1944, 99: 734.
8. Mardomingo, S. G. Las alteraciones hematicas en los traumatismos craneocerebrales. Rev. clín. españ., 1947, 26: 393.
9. Rosenow, G. Untersuchungen ueber die zentralvegetative Blutregulation. Zschr. ges. exp. Med., 1929, 64: 452.
10. Smolik, E. A., Brown, S., and Nash, F. P. Transfusion in the management of closed head injury. South M. J., 1951, 44: 592.

AN EVALUATION OF THE SURGICAL TREATMENT OF CARCINOMA OF THE STOMACH

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MANY SURGEONS are skeptical of the value of total gastrectomy in the treatment of carcinoma of the stomach and believe that the procedure should be employed only when the extensive nature of the neoplasm dictates its use. The principal objections to total removal of the stomach have been high mortality, low survival rate, and adverse nutritional sequelae. At the same time, it has been noted that the survival rate for gastric carcinoma has not changed significantly in recent years. While this latter observation emphasizes the need for continued development of methods of early diagnosis and study of etiologic factors, it seems to suggest also that present methods of treatment should continue to be subjected to critical scrutiny.

Review of several reports concerning the surgical therapy of carcinoma of the stomach has led us to question whether there has been a satisfactory basis for comparing subtotal gastric resection with total gastrectomy in the treatment of gastric carcinoma. Because there has been considerable controversy over this aspect of treatment, the experience on the pavilion service of The New York Hospital has been reviewed. An attempt has been made to correlate this experience with other reports and to indicate where discrepancies lie in interpretation of results.

MATERIAL

Five hundred fifty-seven patients with carcinoma of the stomach were admitted to the pavilion services of The New York Hospital between September 1932 and July 1954. Of these, 358 were men and 199 were women. Their ages ranged from 22 to 81 years. The age distribution by decades is given in Figure 1. The sex and age incidence is not significantly different from other reported series. The majority of patients were in the fifth, sixth, and seventh decades of life.

Only patients in whom a histologic diagnosis was obtained are included in this study.

TREATMENT

Of the 557 patients in this series, 52 patients were not subjected to operation (Fig. 2). Diagnosis in these were established by biopsy of distant metastases and by necropsy.

A laparotomy was performed in 505 patients, or 90 per cent of the entire series. In 151 patients, the procedure was limited to exploration and biopsy, and in 97, a palliative procedure was accomplished.

In 257 patients, removal of the gastric carcinoma was instituted with intent of cure. This number represents 46.1 per cent of the entire series or 50.9 per cent of those patients who were subjected to laparotomy.

Total resection of the stomach was utilized in 38 instances; however, only 2 total gastrectomies were performed during the first 10 year period of this report. Continuity of the gastrointestinal tract was re-established by end-to-side esophagojejunostomy and distal jejunojejunostomy in the majority. Since July 1953, 9 patients have had a segment of jejunum interposed between the esophagus and duodenum (1, 2). Splenectomy was done in conjunction with removal of the stomach in 21 cases, and both partial distal pancreatectomy and splenectomy were associated with 6 total gastrectomies.

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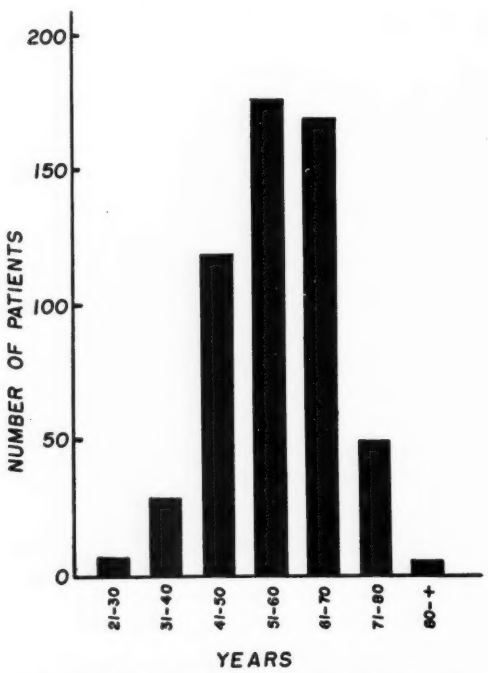

FIG. 1. Age distribution of patients with carcinoma of the stomach at The New York Hospital from 1932 to 1954.

Partial resection of the stomach was performed in 219 patients. In 190 patients, this was a distal resection (partial gastrectomy), while in 29, a proximal resection (esophagogastrectomy) was accomplished. Multiple organ resections were also carried out in this group. Resection of a large segment of the left lobe of the liver was associated with 2 partial gastrectomies and with 2 esophagogastrectomies. In 7 instances, resection of the transverse colon accompanied partial gastrectomy.

TABLE I.—SUMMARY OF OPERATIONS AND OPERATIVE MORTALITY FOR CARCINOMA OF THE STOMACH AT THE NEW YORK HOSPITAL (1932–1954)

	No. of cases	*Postoperative mortality*	
		No.	*Per cent*
No operation	52		
Exploratory laparotomy	151	7	4.6
Palliative operations	97	10	10.3
Total gastrectomy	38	5	13.2
Partial gastrectomy	190	25	13.2
Esophagogastrectomy	29	3	10.3

LOCATION OF THE LESION

The location of the lesions in the stomach in this series is represented graphically in Figure 3. Carcinoma of the antral portion of the stomach was the most frequently encountered. The majority of both partial gastrectomies and palliative operations were performed for lesions arising in this part of the stomach. Eighteen of the 38 patients in whom total gastrectomy was performed had extensive neoplasms which did not permit a less radical procedure. The term extensive lesion was used to designate the neoplasm occupying three-fourths of the stomach.

OPERATIVE MORTALITY

Of the 257 patients who were subjected to definitive resection, 33 died in the period immediately following operation. There were 25 deaths after 190 partial gastrectomies, an operative mortality of 13.2 per cent. Five patients failed to survive 38 total gastrectomies, an operative mortality of 13.2 per cent. Esophagogastrectomy was performed 29 times with 3 deaths, a mortality rate of 10.3 per cent (Table I).

Further analysis has demonstrated an improvement in the operative mortality subsequent to 1941 (Table II). During the first 10 years of this study, 2 total gastrectomies were performed, and both patients died in the immediate postoperative period.

Since 1941, 36 total resections of the stomach have been followed by 3 deaths in the immediate period following operation, an operative mortality of 8.3 per cent. Eleven of the postoperative deaths following partial gastrectomy occurred in the 68 patients operated upon prior to 1942, a mortality rate of 16.2 per cent for this period. Since 1941, 122 partial gastrectomies have been performed with 14 deaths, an operative mortality rate of 11.5 per cent. All of the 29 esophagogastrectomies were performed subsequent to 1941.

SURVIVAL

Fifty-two (9.3 per cent) of the 557 patients who were admitted to The New York

Hospital with carcinoma of the stomach survived 5 years or longer. All patients who were not operated upon or who were subjected only to exploratory laparotomy succumbed in less than 5 years. Of these 89.2 per cent failed to survive 1 year after the diagnosis was established. Among patients in whom palliative procedures were accomplished, only 2 were alive after 5 years. One of these died 5 years after operation with extension of carcinoma. The other was thought to have liver metastases at the time of operation, which was not proved by biopsy, and remains alive and well 10 years following partial gastrectomy.

Of the 257 patients who were subjected to definitive resections, 162 were operated upon prior to July 1, 1949 and survived operation (Table III). Fifty of this group of 162 patients have survived 5 years or longer. One hundred and thirty-three patients were found to have survived partial gastrectomy, and 44 of these lived 5 or more years after operation. Three of the 12 patients who survived total gastrectomy lived 5 or more years. Three of the 17 patients who were subjected to esophagogastrectomy survived 5 or more years.

The adverse effect of lymph node metastasis on survival was noted in the group subjected to partial gastrectomy (Table III). Of the 133 patients eligible for analysis, 70 were not demonstrated to have lymph node metastasis by the surgical pathologist, and 34 (48.6 per cent) lived 5 years or more after operation. However, only 10 of the 63 in whom lymph node metastasis was demonstrated lived 5 years. Conclusions regarding the influence of lymph node metastasis on survival could not be drawn from the other groups because the number of patients was insufficient.

LOCAL RECURRENCE AFTER OPERATION

Local recurrence of carcinoma in the upper gastrointestinal tract was demonstrated in 30 of the 224 patients who survived removal of the gastric neoplasm with curative intent. Twenty-five of these occurred after partial gastrectomy, 4 after esophagogastrectomy, and 1 after total resection of the stomach.

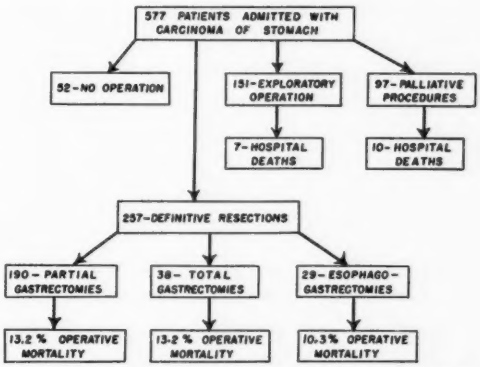

FIG. 2. Summary of treatment for carcinoma of the stomach at The New York Hospital from 1932 to 1954.

The recurrence after total gastrectomy was detected in the esophagus, and the recurrence after other procedures was found in the gastric remnant in each instance. Recurrence was detected by gastrointestinal roentgenograms in 15 cases,[1] visualization by gastroscopy in 1 case, exploratory laparotomy in 7 cases, and by autopsy in 7 cases.

It has been difficult to determine from the records the frequency with which recurrence was localized for a significant period to the gastric remnant. The time interval between the appearance of symptoms and the detection of the recurrent neoplasm varied greatly, and usually definitive studies

[1]Confirmed by gastroscopic examination in 1 case, by exploratory laparotomy in 2 instances, and by autopsy in another.

TABLE II.—OPERATIVE MORTALITY FOLLOWING RESECTIONS FOR CARCINOMA OF THE STOMACH BEFORE AND AFTER 1941 AT THE NEW YORK HOSPITAL

	Subtotal resection	*Total gastrectomy*	*Esophago-gastrectomy*
1932–1941			
No. of operations	68	2	
Operative mortality			
No.	11	2	
Per cent	16.2	100	
1942–1954			
No. of operations	122	36	29
Operative mortality			
No.	14	3	3
Per cent	11.5	8.3	10.3

TABLE III.—FIVE YEAR SURVIVAL AFTER RESECTION FOR CARCINOMA OF THE STOMACH AT THE NEW YORK HOSPITAL (1932–1949)

	No. of operations	*Five year survival*	
		No.	*Per cent*
Subtotal resection	133	44	33.1
Without node metastasis	70	34	48.6
With node metastasis	63	10	15.9
Total gastrectomy	12	3	25
Esophagogastrectomy	17	3	17.6
Total	162	50*	30.8

*This figure does not include 2 patients who survived 5 years after palliative partial gastrectomy.

were undertaken after a period of several weeks from the onset of symptoms. As a result, it was often difficult to determine whether the recurrence represented the focus of spread to the remainder of the upper abdominal cavity or whether the involvement of the stomach was secondary to carcinomatous invasion from adjacent structures.

In the group of 14 patients in whom local recurrence was demonstrated by gastrointestinal roentgenograms, gastroscopy, esophagoscopy, or cytologic examination, jaundice was present in 2 and ascites in a third. Among 14 other patients, local recurrence with visceral extension was found at autopsy in 7 and at the time of laparotomy in 7. One of the latter group was subjected to total gastrectomy, transverse colectomy, and partial pancreatectomy for recurrent carcinoma which extended into the structures removed. The patient succumbed during the immediate postoperative period.

One patient died 3 years following partial gastrectomy and at autopsy was found to have a neoplastic mass involving the remainder of the stomach with direct extension to the spine. There was no other visceral involvement or distant metastasis.

TABLE IV.—WEIGHT CHANGE FOLLOWING RESECTIONS FOR CARCINOMA OF THE STOMACH

	Partial gastrectomy	*Total gastrectomy*	*Esophagogastrectomy*
	No.	*No.*	*No.*
Total number of patients	35	11	6
Weight above preop. level	11	2	0
Weight equal to preop. level	8	4	3
Weight below preop. level	16	5	3
Regained usual weight	10	1	1
Weight below usual level	25	10	5

In 1 patient, local recurrence in the gastric remnant was detected 2 years after partial gastrectomy. The recurrence was confined to the stomach without demonstrable lymph node metastasis. This patient has survived more than 6 years after total gastrectomy and splenectomy without further evidence of disease.

NUTRITIONAL ASPECTS

Considerable emphasis has been placed upon the occurrence of malnutrition following removal of the entire stomach. Few observations have been made relating to nutritional disturbances after partial gastrectomy for carcinoma, although several reports have appeared which indicate that some degree of nutritional abnormality occurs in from 42 to over 75 per cent of patients after partial gastrectomy for peptic ulcer.

Because there is a lack of information, an attempt has been made to assess the effects of the various types of resections in this series upon the nutritional status of the surviving patients. Digestive disturbances, weight changes, and activity of the patients have been studied. Patients were included in this analysis who had survived long enough so that weight and activity status could be determined. In addition, an effort was made to exclude recurrence of carcinoma as a factor because this is known to be associated with weight loss and malnutrition. Weight changes were correlated with weight before operation and with the usual weight of the patient. Although the methods outlined are not precise, the information provided an estimate of relative changes in nutritional status following resection.

Sufficient information concerning weight changes was obtained in 35 patients who had been subjected to partial gastrectomy and who had survived from 2 to 10 years after operation without evidence of recurrence (Table IV). Eleven patients had gained weight in excess of the level before operation, and this gain represented a return to the usual weight level in 10 of these patients. Twenty-five patients (71 per cent)

remained below their usual weight, and 16 of these had failed to regain their preoperative weight.

Eleven patients were followed from 1 to 7 years after total gastrectomy without evidence of recurrence during the period of observation of weight change. Two of these were found to have gained weight in excess of the operative level, and 1 had returned to his usual level. Four of the 11 had regained the weight of the preoperative period. However, 10 remained below their usual weight status.

Only 6 of the esophagogastrectomy group were suitable for analysis. Three remained below the preoperative level, and 5 were below their usual weight.

The status of digestive function was somewhat more difficult to determine (Table V). There was considerable variation in subjective symptomatology of these patients, and it is also apparent that much depends upon the impression of the examiner. As a result, the digestive disturbances have been grouped in a broad classification according to severity. Patients who had mild epigastric distress or a sensation of distention but who were able to eat a relatively unrestricted diet were classified as having mild symptoms. Patients who had postprandial nausea or occasional vomiting, regurgitation, epigastric distress, and who had dietary restrictions, were considered to have moderately severe digestive symptoms. Those who complained of weakness, epigastric distress, sweating, fainting, and required several small meals daily were placed in the category of marked disturbance.

It was found that nearly one-half of the patients who had been subjected to partial gastrectomy had definite digestive disturbances which were elicited by interview. Weight gain was also limited in this group. Seven of the 9 patients with total resection of the stomach had postprandial symptoms, and in 1 the symptoms were severe.

Determination of activity proved to be unsatisfactory. In 4 of the patients, information on work status was lacking in the record

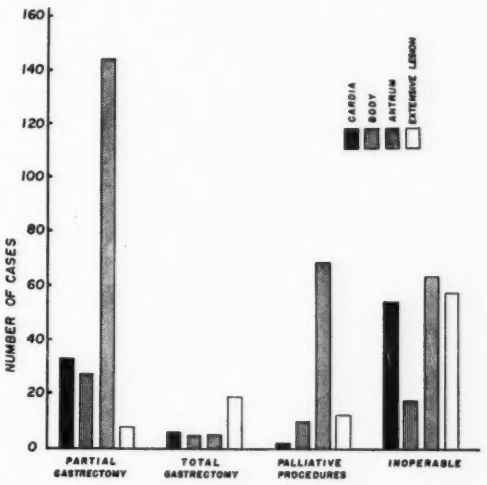

FIG. 3. Relation of treatment of carcinoma of stomach to location of lesion (The New York Hospital from 1932 to 1954).

during the period of analysis, and they are not available at present for study. Eight patients had retired because of age. Of the remaining patients, there was no significant difference between the three groups although the patients who had been treated by total gastrectomy were slower to return to activity.

DISCUSSION

Evaluation of operative procedures must include not only consideration of ultimate arrest of the disease process but must include an examination of operative mortality and morbidity. The operative mortality for major surgical procedures has been progressively reduced in recent years, and this is reflected in the operative results in the present series. The operative mortality for partial

TABLE V.—DIGESTIVE COMPLAINTS FOLLOWING RESECTIONS OF THE STOMACH FOR CARCINOMA

Type of resection	*Total patients studied*	*—Degree of digestive disturbances— Minimal or absent*	*Mild*	*Moderate*	*Marked*
Partial gastrectomy...	35	19	3	7	6
Total gastrectomy....	11	2	4	2	1
Esophagogastrectomy.	6	3	0	1	1*

*One additional patient had dysphagia due to stricture of esophagogastric junction.

gastrectomy was 16.2 per cent prior to 1942 and subsequently has fallen to 11 per cent. During the same period, the mortality rate for total gastrectomy fell from 100 to 8.3 per cent. It is to be noted, however, that the operative mortality for total gastrectomy is based on 36 cases while that for partial gastrectomy is obtained from 122 operations. A similar relationship is found in the series reported in 1954 by Marshall and Uram who recorded an operative mortality of 8.7 per cent for 127 total gastrectomies and 6.7 per cent for 371 partial gastrectomies. While in most clinics the mortality rate for partial gastrectomy is less than that of total gastrectomy, it is apparent that the mortality rate for total gastric resection has improved with a larger number of cases in the hands of experienced surgeons and does not greatly exceed that of partial gastrectomy.

There is no question that total gastrectomy is an operation of greater magnitude than partial gastrectomy. The catabolic response elicited by total resection is greater, and this is reflected in the length of hospitalization which is usually more prolonged in such patients. It would appear from the mortality figures that this should not represent a determining factor in the choice of operative procedure except in those cases in which a serious complicating disease process is present, such as advanced cardiac disease. With better understanding of blood volume, fluid and electrolyte correction before operation, and intelligent management after operation, the majority of patients can tolerate operations of greater magnitude.

A minor objection to total gastrectomy has been related to the physiologic disturbances that result from removal of the entire stomach. Total gastrectomy results in the development of macrocytic anemia in practically all instances unless proper therapy is instituted. This condition seems to be related to failure of vitamin B_{12} absorption. This hematopoietic problem can be adequately corrected or prevented by appropriate substitutional therapy.

Objectionable regurgitation of bile and intestinal contents has been overcome by the use of an enteroenterostomy distal to the esophagojejunostomy, by Roux-Y esophagojejunostomy, and, more recently, by interposing segments of the intestinal tract between the esophagus and duodenum (1, 2). These measures diminish and prevent esophagitis and jejunitis in most cases.

However, the principal criticism by many is focused on nutritional disturbances after total gastrectomy. Evaluation of nutritional status is often difficult in patients who have been subjected to gastrectomy for carcinoma of the stomach because recurrence of the malignant neoplasm produces weight loss, digestive symptoms, and malnutrition. This is an important consideration when it is recalled that most reports state that total gastrectomy has been performed for extensive lesions and that few 5 year survivals have been obtained. It is apparent from the findings in our series that partial gastrectomy is associated with impairment of gastrointestinal function in a significant number of patients. More than two-thirds of the patients after partial gastrectomy in the present series had sufficient malfunction of the gastrointestinal tract to be reflected in lack of weight gain or subjective digestive disturbances. This correlates well with the observations of Zollinger and Ellison who found that approximately two-thirds of their patients failed to attain their minimal ideal weight after conventional resections for peptic ulcer. Presumably, many subtotal resections for carcinoma are more extensive than those performed for peptic ulcer, and an even higher incidence of diminished weight gain might be expected.

Studies of alimentary tract function on patients with subtotal resections and with total gastrectomy have demonstrated that there is a decreased transit time for ingested substances and that absorption of carbohydrate, protein, and fat is diminished. Hypertonic solutions introduced by the oral route have been shown to produce a fall in plasma volume, electrocardiographic chang-

es, and distention of the upper small bowel which can be correlated with symptoms classed under the "dumping syndrome." With a background provided by such basic studies as these, and with increased awareness of the nutritional problems confronting patients after gastrectomies of all types, it is now possible to manage such problems with greater facility in the majority of cases.

It is seldom, with proper management after total gastrectomy, that gastrointestinal function is disturbed sufficiently that patients are prevented from resuming gainful employment or useful activity. This finding is corroborated by the report of ReMine and Priestley who found that only 1 of 13 was incapacitated in the group who survived 5 years after total resection of the stomach.

From the standpoint of definitive therapy of carcinoma of the stomach, it would appear, therefore, that technical difficulties, morbidity, operative mortality, and physiologic consequences are not of sufficient magnitude to preclude the use of total gastrectomy as a preferred method in surgical treatment of gastric carcinoma if its value can be demonstrated as a curative measure. There has been general pessimism expressed over the paucity of long term survivals after total gastrectomy for carcinoma of the stomach. This would appear to be the result of the type of lesion which has been subjected to this more radical resection. In our series, 18 of the 38 patients who were treated by total gastrectomy were found to have extensive neoplastic involvement of the stomach. ReMine and Priestley reported that "diffuse lesions" were present in 50 per cent of the 170 cases of total gastrectomy for malignant lesions. Marshall and Uram stated that the results of total and partial gastrectomy for carcinoma cannot be compared because these operations were not done for comparable lesions.

In the present series, the finding that 3 of 12 patients who were eligible for survival lived more than 5 years after total gastrectomy is encouraging. While total gastrectomy has certain anatomic limitations in eradication of lymphatic metastases, it has been demonstrated that more lymph nodes are removed with total resection of the stomach than with partial resection. The striking incidence of recurrence in the gastric remnant after partial gastrectomy merits further consideration and would appear to be a strong argument in favor of complete extirpation of the stomach.

From the considerations which have been presented, it seems that more extensive experience with total gastrectomy is warranted in institutions where sufficient material and experience permit the performance of the operation with reasonable mortality and morbidity. An accurate appraisal awaits an objective analysis of a larger number of cases of total gastrectomy which have been performed for lesions of a less extensive nature.

SUMMARY

The surgical treatment of carcinoma of the stomach at The New York Hospital from 1932 to 1954 has been reviewed. Partial gastrectomy was utilized 190 times with intent of cure with an operative mortality of 13.2 per cent. There was a 33.1 per cent 5 year survival rate for the 133 patients who survived definitive operations and who were eligible for 5 year survival analysis. During the same period, 38 total gastrectomies were performed for carcinoma with 13.2 per cent mortality after operation. Three of the 12 patients who survived operation prior to July 1, 1949 lived for more than 5 years. Esophagogastrectomy was employed in 29 cases with an operative mortality of 10.3 per cent. Three of the 17 eligible patients who recovered from operation lived more than 5 years.

Analysis of the series demonstrated that the lesions for which total gastrectomy was performed were much more extensive than those for which partial resection of the stomach was undertaken. The incidence of local recurrence of carcinoma and of abnormal alimentary tract function has been analyzed and discussed. It has been concluded that the efficacy of total gastrectomy cannot be adequately assessed on the basis of available information. In view of decreasing operative

mortality and better understanding of the management of gastrointestinal sequelae, a more extensive trial of total gastrectomy should be undertaken in the treatment of more favorable lesions.

REFERENCES

1. Beal, J. M., Briggs, J. D., and Longmire, W. P., Jr. Use of jejunal segment to replace the stomach following total gastrectomy. Am. J. Surg., 1954, 88: 194–199.
2. Longmire, W. P., Jr., and Beal, J. M. Construction of a substitute gastric reservoir following total gastrectomy. Ann. Surg., 1952, 135: 637–645.
3. Marshall, S. F., and Uram, H. Total gastrectomy. Surg. Gyn. Obst., 1954, 99: 657–675.
4. ReMine, W. H., and Priestley, J. T. Late results after total gastrectomy. Surg. Gyn. Obst., 1952, 94: 519–525.
5. Zollinger, R. M., and Ellison, E. H. Nutrition after gastric operations. J. Am. M. Ass., 1954, 154: 811–814.

METASTASIS TO THE REGIONAL NODES OF THE SPLENIC HILUS FROM CARCINOMA OF THE STOMACH

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EVEN THOUGH the clinical and pathologic picture of carcinoma of the stomach was first described by Avicenna (21) in the eleventh century A.D., it was not until Billroth (21) performed the first successful partial gastrectomy for this entity in 1881 that an active approach to its treatment became possible. The importance of the lymphatic spread of carcinoma of this organ was recognized as early as 1900 by Cunéo. He and Jamieson and Dobson, Delamere, Poirier, and Cunéo, and Rouvière have contributed the bulk of our present knowledge of the lymphatic system. All described the group of regional nodes situated near the hilus of the spleen, but it remained for Coller, Kay, and MacIntyre to indicate the importance of this particular group of nodes in relation to gastric carcinoma. Lahey and Marshall, at about the same time, indicated that the addition of splenectomy to total gastrectomy facilitated the latter procedure, and also did not materially increase the operative mortality. About a year later, Garlock noted that the pancreaticolienal group of nodes was one of the major areas of spread of gastric carcinoma. It is surprising that during the ensuing 12 years, only the reports of Eker and of Sunderland and associates have re-emphasized the importance of this group of nodes, even though Brunschwig, in 1948, advocated splenectomy and partial pancreatectomy with gastrectomy for carcinoma of the stomach with invasion of the pancreas. Walters, Gray, and Priestley (22), McNeer and co-workers, Sweet, ReMine and Priestley, and many others have since suggested the inclusion of these organs in gastrectomy for localized lesions. Lewis and Wangensteen have recently reported that they remove the spleen and areas of drainage to the suprapancreatic lymph nodes as a routine in operations for any gastric carcinoma.

The purpose of this study was to evaluate the importance of the group of regional nodes situated in and near the hilus of the spleen.

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MATERIALS AND METHODS

The case records of all patients who had undergone gastrectomy with concomitant splenectomy for carcinoma of the stomach at the Mayo Clinic during the 7 year period from 1946 through 1952 were reviewed. From this group, 102 available surgical specimens were selected for study on the basis of the following criteria: (1) the malignant process was primarily of the stomach; (2) a concomitant splenectomy had been performed at the time of gastrectomy, regardless of the reason; (3) sufficient tissue was present in the splenic pedicle for examination. All of the surgical specimens were preserved in a 10 per cent formalin solution.

Grossly, the specimens were classified according to the systems of Borrmann and coworkers and of Dukes as modified by Dochat. The gross characteristics of the lesions were catalogued as ulcerative, polypoid, scirrhous, or otherwise. The greatest transverse diameter of each lesion as recorded in the report of the pathologist who examined the fresh specimen was determined. Finally, the location of the lesion, whether in the proximal or distal segment of the stomach, was determined.

TABLE I.—CORRELATION OF NODAL INVOLVEMENT WITH TYPE OF SURGICAL PROCEDURE IN 102 PATIENTS WITH GASTRIC MALIGNANCY

Operation	*Total cases*	*Regional nodes, cases*			
		Splenic hilar			*Not*
		Involved	*Per cent*	*Involved**	*involved*
Subtotal gastrectomy..	11	4	36.4	8	3
Total gastrectomy....	66	27	40.9	56	10
Esophagogastrectomy.	25	6	24.0	21	4
Total.....	102	37	36.3	85	17

*Includes splenic hilar nodes in Tables I, II, and III.

The nodes at the hilus of the spleen, the subpyloric nodes, and those on the greater curvature and lesser curvature of the stomach were identified and studied. The splenic hilar group was considered to include the nodes found in the splenic pedicle, the gastrolienal ligament, and the pancreaticolienal ligament, within 2 centimeters of the spleen. The subpyloric nodes were those below and adjacent to the pylorus and along the distal 2 to 3 centimeters of the greater curvature. Designated as nodes of the greater curvature were those found near the gastroepiploic vessels between the leaves of the gastrocolic omentum and adjacent to the greater curvature. These were called "inferior gastric" by Sunderland and associates. Listed as nodes of the lesser curvature were those along the right and left gastric artery and its branches coursing along the lesser curvature between the layers of the lesser omentum. These were called "superior gastric" by Sunderland and associates.

All of the nodes from the region of the splenic hilus were prepared in permanent section. In the remainder of the regions, nodes were examined by the frozen section technique and fixed sections of all questionable or positive nodes were then prepared. All these sections were stained with hematoxylin and eosin. No attempt was made to examine all nodes in the regions, other than the splenic hilus, once a positive node was found.

The method of cytologic grading which was first described by Broders in 1921 (2), and modified by him in 1925 (3) and again in 1941 (4) was used throughout the present study.

CLINICAL FINDINGS

Age and sex incidence. The average age of the patients in this series was 58.79 years, with a range of 32 to 80 years. Seventy per cent of the patients were in the sixth and seventh decades. There were 79 males and 23 females, a ratio of 3.4 to 1.

Duration and character of symptoms. The duration of symptoms ranged from no symptoms referable to the gastrointestinal tract in 1 case to 36 months in another. The average duration was 8.48 months. No significant difference in the duration of symptoms was observed between patients with any nodal involvement and those which also included involvement of the splenic hilar nodes. Dysphagia was noted in 28 cases; in all 28 the tumors involved the proximal half of the stomach. This was the only symptom in 14 of the patients. The most common complaints were burning, pain, cramps, or soreness in the epigastric region (41 cases), and epigastric fullness or a sensation of filling easily or quickly (33 cases). Bleeding was uncommon either alone or associated with any other symptom.

Physical examination. The only significant physical findings were loss of weight, the presence of an epigastric mass, and some degree of epigastric tenderness. One or more of these were found in 80 per cent of the patients. There was no history of loss of weight in 21 cases, but in the remainder it ranged from 4 to 60 pounds, an average of 19.5 pounds. An epigastric mass was palpable in only 19 patients, all of whom indicated some degree of tenderness.

Laboratory findings. The gastric contents of 65 patients had been analyzed; 49 had no free hydrochloric acid. Of the remaining 16 patients, only 4 had more than 30 units of free hydrochloric acid. On admission 19 patients were found to have less than 10 grams of hemoglobin per 100 cubic centimeters of blood. Roentgenologic examinations of the upper part of the gastrointestinal tract were interpreted as being positive for carcinoma in 66 per cent, and in an additional 28 per cent as indicating surgical exploration.

SURGICAL CONSIDERATIONS

The patients in this series had undergone one of three types of operative procedures, in addition to splenectomy. Total gastrectomy was performed on 66 patients, subtotal gastrectomy on 11, and esophagogastrectomy, including removal of the upper segment of the stomach and from 1 to 6 centimeters of esophagus, on 25. In no instance was the spleen included in the resection, primarily because of clinical evidence of metastasis. In 1 case the spleen was removed because invasion of the gastrolienal ligament by the malignant lesion was suspected by the surgeon but the lesion in this structure proved to be inflammatory on histologic examination. In the remainder, the spleen was removed to facilitate the procedure or to control bleeding (Table I).

PATHOLOGIC FINDINGS

Nodal involvement. In 17 specimens, 16.7 per cent of the total, no nodal involvement was found. In the remaining 85 specimens from 1 to 4 of the regional groups of nodes investigated were involved, and the hilar nodes of the spleen were found to be involved in 37 (43.5 per cent) of this group. In 2 specimens, both with lesions located in the region of the cardia, the only nodal involvement found was in the splenic hilar group. In the 25 cases in which esophagogastrectomy was performed, the specimens contained no tissue from the region of the subpyloric group of nodes; therefore, only nodes from three zones were studied.

Location of the lesion. On the basis of gross and microscopic involvement of the gastric wall (Table II) the involvement was predominantly in the proximal half of the stomach in 66 specimens, in the distal half in 20, and in all of the stomach or in part of both segments in 16. The multiple primary carcinomas, of which 3 were found in the series, were included in this last group. The involvement of the proximal half of the stomach in 64.7 per cent of specimens and the distal half in 19.6 per cent is a reversal of the overall incidence in cases of gastric carcinoma. This, of course, would be expected in a series in which the spleen was required as a part of the specimen to meet the criteria of selection of cases for study and in which about 90 per cent of the specimens were removed at total gastrectomy or at esophagogastrectomy. The preponderance of total gastrectomy also indicates that the lesions were relatively extensive.

TABLE II.—CORRELATION OF NODAL INVOLVEMENT WITH LOCATION OF GASTRIC CARCINOMA

		Regional nodes, specimens			
	Total	*Splenic hilar*		*Not*	
Location in stomach	*specimens*	*Involved*	*Per cent*	*Involved*	*involved*
Distal half	20	6	30.0	15	5
Proximal half	66	25*	37.9	56	10
More than 80 per cent involved	16	6	37.5	14	2
Total	102	37	36.3	85	17

*In 2 specimens, only the splenic hilar nodes were involved.

The 20 cases in which the lesions were located in the distal half of the stomach are of special importance, as subtotal gastrectomy without splenectomy is commonly selected for this type of lesion as the procedure of choice. The splenic hilar nodes were involved in 6 cases (30 per cent of this group, and 40 per cent of the 15 cases in this group in which malignant nodes were found). Ten of the specimens in which the lesions were located in the distal half of the stomach were removed by subtotal gastrectomy; and in 3 of these 10, splenic hilar nodes were involved. This group will be considered in more detail later.

Size of the lesion. The size of the lesion was determined from measurements made of the fresh specimen and noted on the pathologic report; only the greatest diameter mentioned was used. The greatest diameter varied from 3 centimeters to the entire gastric wall (Table III). Sixty-four of the specimens contained lesions 11 centimeters or less in diameter, and 38 contained larger lesions. The multiple primary malignant lesions are included in the latter category. The incidence of splenic hilar nodal involvement is significantly greater in the lesions more than 11 centimeters in diameter, being 47.4 per cent as compared to 29.7

TABLE III.—CORRELATION OF NODAL INVOLVEMENT WITH DIAMETER OF GASTRIC CARCINOMA

Diameter of gastric lesion, cm.	*Total specimens*	*Regional nodes, specimens*			
		Splenic hilar Involved	*Per cent*	*Involved*	*Not involved*
3–7	31	8*	25.8	25	6
8–11	33	11	33.3	28	5
More than 11	35	16	45.7	30	5
Multiple	3	2	66.7	2	1
Total	102	37	36.3	85	17

*In 2 specimens, only the splenic hilar nodes were involved.

per cent in the lesions 11 centimeters or less in diameter. However, in 2 of the 31 specimens with lesions from 3 to 7 centimeters in diameter, the splenic hilar nodes were the only ones involved. In both of these specimens the lesions were in the region of the cardia and both had been removed at esophagogastrectomy. By contrast, in the total series, involvement of unspecified groups of nodes by the lesions 11 centimeters or less was not significantly different from that by lesions greater than 11 centimeters, as it was 82.8 per cent and 84.2 per cent, respectively. From these data it appears that, whereas the splenic hilar nodes are likely to be involved much oftener by extensive gastric lesions, they also are involved in a significant percentage of the smaller lesions, and involvement of any of the other groups of regional nodes cannot be considered as indicating a likelihood of splenic hilar metastasis.

Local invasion of the primary lesion. Eleven of the lesions had not invaded any structure outside the gastric wall. The peritoneum only was invaded in 35 specimens. Additional nearby structures, including esophagus, duodenum, pancreas, colon, jejunum, diaphragm, gastrohepatic ligament, gastrocolic ligament, gastrolienal ligament, and liver, as well as the peritoneum were invaded in 56 specimens (Table IV). In 14 of the 37 specimens exhibiting splenic hilar nodal involvement, the peritoneum only was invaded locally; in the remaining 23 specimens, additional invasion of nearby structures had occurred. In 6 specimens, the gastrolienal ligament was invaded but the nodes were involved by metastasis rather than by direct extension, and in 1 specimen, the gastrolienal ligament was invaded without involvement of the splenic hilar nodes. As said before, in the 1 case in which the spleen was removed with the stomach because invasion of the gastrolienal ligament was suspected, only inflammatory changes were found on microscopic examination.

TABLE IV.—CORRELATION OF NODAL INVOLVEMENT WITH INVASION OUTSIDE THE GASTRIC WALL

	Specimens	*Invasion, specimens*					
		None		*Peritoneum only*		*Any structures**	
		No.	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*
No nodes involved	17	4	23.5	2	11.8	13	76.5
Any nodes involved	85	7	8.2	33	38.8	78	91.8
Total	102	11	10.8	35	34.3	91	89.2
Splenic hilar nodes involved	37	0	—	14	37.8	37	100.0

*Includes peritoneum, esophagus, duodenum, pancreas, colon, jejunum, diaphragm, gastrohepatic ligament, gastrocolic ligament, gastrolienal ligament, and liver.

Involvement of nearby structures was not significantly related to the degree of nodal involvement. Thus, local invasion had occurred in 76.5 per cent of specimens in which no nodes were involved, whereas in 91.8 per cent of specimens in which any of the four groups of nodes were involved and in 100 per cent of the group in which splenic hilar nodes were involved, with or without other groups of nodes, local invasion had occurred.

Gross classification. In 72.8 per cent of the specimens the lesions were ulcerative; all specimens which gave gross evidence of ulceration were included. In 16.5 per cent the lesions were scirrhous, in 8.7 per cent polypoid, and in 1 case there was carcinoma en nappe. The splenic hilar nodes were involved by 34.7 per cent of the ulcerative lesions, by 52.9 per cent of the scirrhous lesions, by 11.1 per cent of the polypoid lesions, and in the 1 case of carcinoma en nappe.

Four specimens were classified as type A (Dukes' classification), 13 as type B, and the remainder as type C; by definition all so classed had nodal involvement.

On the basis of Borrmann's classification, 10 specimens were classified in groups 1 and 2, 45 in group 3, and 47 in group 4. The hilar nodes of the spleen were involved twice as frequently by the lesions of group 4 as by those of groups 2 and 3; no splenic hilar nodes were involved in the 3 cases classified as group 1.

Microscopic grade of malignancy. The distribution by grade (Broders' classification of malignancy) is consistent with other reported series of carcinoma of the stomach, there being a marked predominance of the lesions of high grade (Table V). No splenic hilar involvement was found in the 3 specimens in which the carcinoma was graded 1; it was found in 2 of the 13 specimens containing carcinomas of grade 2, in 8 of the 33 lesions of grade 3, and in 27 of the 53 specimens containing lesions of grade 4. It is generally accepted that lesions of the higher grade are more likely to spread to regional nodes, and this seems to hold true for the splenic hilar group of nodes also.

Regions involved. In 37 of the 85 specimens exhibiting nodal involvement, the splenic hilar nodes were involved metastatically. In 2 specimens, only the splenic hilar group of nodes was involved, and in both, the primary lesions involved the upper half of the stomach. In 23.6 per cent of the specimens in which splenic hilar nodes were involved, one other group of nodes was involved; in 42.1 per cent two other groups were involved, and in 29.0 per cent all four groups were involved. The incidence of splenic hilar involvement alone is small, but that it does occur should be given consideration, especially when the lesions are in the proximal half of the stomach. If any group of nodes is involved in a specimen containing any but a very small lesion in the distal portion of the stomach, there is about a 45 per cent chance that the splenic hilar nodes will be involved.

Number and size of splenic hilar nodes. A total of 301 nodes was found in the splenic hilar regions in all specimens, an average of 2.9 nodes per case. In the 37 specimens with positive splenic hilar nodes, 104 nodes were found, an average of 2.8 nodes per specimen. Of these, 68 nodes were metastatically involved, an average of 1.8 nodes per specimen.

TABLE V.—CORRELATION OF NODAL INVOLVEMENT WITH DEGREE OF MALIGNANCY OF GASTRIC LESION (BRODERS' CLASSIFICATION)

		Regional nodes, specimens			
		Splenic hilar			
Grade	*Total specimens*	*Involved*	*Per cent*	*Involved*	*Not involved*
1	3	0	—	1	2
2	13	2	15.4	9	4
3	33	8*	24.2	30	3
4	53	27	50.9	45	8
Total	102	37	36.3	85	17

*In 2 specimens, only the splenic hilar nodes were involved.

The greatest transverse diameter of all involved splenic hilar nodes was measured on cut section from the fixed specimen. The range was 1 to 8 millimeters with an average of 3.6 millimeters. The diameter of the uninvolved nodes in the splenic hilar region in association with involved nodes averaged 2.8 millimeters, while the average diameter of all splenic hilar nodes in the specimens was 3.7 millimeters.

The greatest transverse diameter of 10 (14.7 per cent) of the 68 involved splenic hilar nodes was less than 1.5 millimeters. In 9 of the specimens, the only involved splenic hilar nodes were 2 millimeters or less in diameter. All the involved nodes then were very small, and the involvement in many of these nodes was very early, as only a small number of malignant cells were found in the sinusoids of the nodes. It is obvious, therefore, that in many of these cases, a diagnosis of metastasis would have been impossible for the surgeon to make by inspection and palpation.

Splenic hilar nodal involvement in specimens removed at subtotal gastrectomy. Subtotal gastric resection without splenectomy is the procedure usually employed for carcinoma of the distal segment of the stomach. In 1 of the 11 cases in this series in which the spleen had been removed at the time of a subtotal gastrectomy either to facilitate exposure or because of bleeding from the cap-

sule, the operation was considered to be palliative because of peritoneal implants. This case will not be considered further. The remaining 10 cases, even though the number is small, are of real consequence because this type of lesion is likely to be removed by subtotal gastrectomy without associated splenectomy. In 3 of these 10 cases splenic hilar nodes were involved. The primary lesion was in the distal half of the stomach in each of the 3 specimens and was less than 7 centimeters in greatest transverse diameter. Two of the lesions were carcinoma, grade 3 (Broders), and 1 was carcinoma, grade 4. In each of the 3 specimens, other groups of nodes were involved and there was invasion of the peritoneum.

It is well known that about three-fourths of the gastric malignant lesions occur in the distal half of the stomach and that the majority of these lesions are treated by subtotal gastrectomy with wide resection of the node-bearing regions, exclusive of the splenic hilar nodes. The finding of metastasis to the splenic hilar node in 30 per cent of this small series indicates the necessity for en masse removal of the spleen as a routine procedure whenever subtotal or total gastrectomy is carried out for cancer of the stomach. Concomitant removal of the spleen does not materially increase the operative mortality or the postoperative morbidity. The splenic hilar group of nodes has received too little attention in the past, especially when the malignant lesions are in the distal half of the stomach. This study indicates that en masse splenectomy is one of the easiest methods of improving results of the surgical treatment of cancer of the stomach.

COMMENT

Curative surgery for carcinoma of the stomach has for its objective complete removal of malignant cells, whether confined to the primary lesion or also present in the regional lymph nodes. The choice of total versus subtotal gastrectomy for eradication of the primary lesion is indicated principally by the surgeon's findings with regard to the extent of submucosal spread. His observations can be confirmed or negated before operation is completed in centers where the surgical pathologists give dependable, immediate reports from study of frozen sections of multiple areas taken from the proximal and distal edges of the resected specimen. However, regardless of the width of cancer-free gastric "cuffs," the nodes along the gastric arteries, in the region of the pylorus, and along the greater curvature of the stomach must be included in resections for carcinoma, together with the greater and lesser omentum and as many of the ligamentous attachments of the stomach as possible. It is believed that the outlook could be improved if it were possible to remove the nodes along the hepatic artery and the celiac axis. It is indeed surprising, therefore, that so little attention has been given to the splenic hilar group of nodes as possible avenues of spread.

Even as late as 1941, when Coller, Kay, and MacIntyre noted a 17.5 per cent involvement of the pancreaticolienal nodes in a series of cases of carcinoma, they suggested that their finding was of little importance because the lesions which metastasized to this group comprised the small minority found in the fundus and cardia. Eker, in 1951, studying a series of specimens obtained at total gastrectomy which included the spleen found that the splenic hilar nodes were involved in 21.7 per cent. However, most importantly, the lesions located in the distal half of the stomach were responsible for involvement of this group of nodes in 18.8 per cent of the specimens. Sunderland and co-workers, in 1953, noted involvement of the splenic hilar nodes in 37.1 per cent of 35 specimens with nodal involvement and concluded that the high incidence of metastasis to the pancreaticolienal group of nodes (including splenic hilar and peripancreatic) was the most significant feature in their study.

The splenic hilar nodes were involved in 43.5 per cent of our 85 specimens with

nodal metastasis and in 36.3 per cent of the total 102 specimens. In both this series and that of Sunderland and co-workers a majority of lesions involved the proximal segment or the entire stomach. It might accordingly be presumed that this site of the carcinoma is the cause of the high incidence of involvement of the splenic hilar nodes. However, even though the number of specimens with nodal involvement in which the lesion was located in the distal segment of the stomach is relatively small, the finding of splenic hilar involvement in 6 of the 15 cases (40 per cent) in this group with nodal involvement is of great significance. Surprisingly enough, the size of the gastric lesion was not a major factor in nodal involvement of the splenic hilar nodes in this small group with lesions in the distal half of the stomach. This is indicated by the fact that the lesion in the stomach in only 1 of the 6 specimens with involved splenic hilar nodes was more than 7 centimeters in greatest diameter, and that 4 of these 6 specimens were removed by subtotal gastrectomy. In 2 specimens all four groups of nodes were involved, in 2 specimens three groups, and in the remainder, two groups were involved. This does not prove that retrograde metastasis did not occur, but the lesions were not of the extent usually seen in association with such spread. In none of these cases was it evident grossly that the spleen needed to be removed and indeed, in only 1 case was an involved node as large as 6 millimeters in diameter found. In 1 specimen of this group, the largest involved node was 1.5 millimeters in diameter, and in the remainder the diameters ranged up to 5 millimeters. In a majority of the nodes only very early involvement was found with cells or groups of cells noted in the sinusoids only.

Selection of cases is an important factor in a study of this type when inclusion of splenectomy with gastrectomy is a criterion. It has not been common practice to include the spleen in subtotal gastrectomy for carcinoma of the distal segment of the stomach. In the period and series under consideration herein, the ratio of total or proximal subtotal gastrectomy or esophagogastrectomy to ordinary subtotal gastrectomy for carcinoma of the stomach was reversed from that in the usual series.

Since total and proximal subtotal gastrectomies were preponderant in our group, inclusion of the spleen in the operation may indicate a more extensive lesion than in most cases even though 62.7 per cent of the specimens exhibited lesions 11 centimeters or less in diameter. That size is of little significance in nodal involvement is indicated by the incidence of such involvement in 82.8 per cent of the lesions 11 centimeters or less in diameter and 84.2 per cent in lesions over this size. However, splenic hilar nodes were involved in a significantly higher percentage in the more extensive lesions.

Splenic hilar nodes were involved twice as often by carcinoma, grade 4, as by that of grade 3, even though the incidence of involvement of some nodes is not significantly different in these two grades of gastric carcinoma.

The incidence of splenic hilar involvement in scirrhous carcinoma of 52.9 per cent as compared to 11.1 per cent in the polypoid group reflects a higher grade of malignancy and a greater propensity of the former to spread. The 10 cases considered pertinent in which subtotal gastrectomy was performed, even though few, are mentioned again because of the great importance attached to finding involved splenic hilar nodes in 3 instances. For gastric lesions of the type present in these 10 cases, subtotal gastrectomy is feasible and the spleen is not ordinarily removed. It is immediately apparent that in some of the cases in which a cure is thought to be accomplished by subtotal gastrectomy failure occurs because the spleen and adjacent nodes are allowed to remain.

Since no small prepyloric lesions or early malignant gastric ulcers were included in our series, no conclusion can be drawn in regard to this type of lesion.

CONCLUSIONS

On the basis of this study and of the reports of others in the literature, it is believed that lymph nodes located in and near the hilus of the spleen are important sites for spread of gastric carcinoma. Until diagnostic methods are developed which will bring victims in the earliest stages of this disease to the surgeon, the attack will continue to be on the primary lesion and the regional lymph nodes. Since the spleen is considered an "unnecessary" organ, and since its removal does not materially increase the operative mortality or postoperative morbidity, it is suggested that the spleen should be removed with the hilar nodes en masse in the course of resection for carcinoma of the stomach.

REFERENCES

1. Borrmann, R. Geschwuelste des Magens und Duodenums. In: Henke, F., and Lubarsch, O. Handbuch der speziellen pathologischen Anatomie und Histologie. Vol. 4, pt. 1, p. 865. Berlin: Julius Springer, 1926.
2. Broders, A. C. Squamous-cell epithelioma of the skin. Ann. Surg., 1921, 73: 141–160.
3. Idem. Grading of carcinoma. Minnesota M., 1925, 8: 726–730.
4. Idem. The microscopic grading of cancer. Surg. Clin. N. America, 1941, 21: 947–962.
5. Brunschwig, Alexander. Pancreato-total gastrectomy and splenectomy for advanced carcinoma of the stomach. Cancer, 1948, 1: 427–430.
6. Coller, F. A., Kay, E. B., and MacIntyre, R. S. Regional lymphatic metastases of carcinoma of stomach. Arch. Surg., 1941, 43: 748–761.
7. Cunéo, B. Quoted by Jamieson and Dobson (13).
8. Delamere, G., Poirier, P., and Cunéo, B. The Lymphatics. London: Constable & Co., Ltd., 1913.
9. Dochat, G. R. A prognostic comparison of serosal and nodal spread in carcinoma of the stomach, with a classification into Dukes' types. Thesis, Graduate School, University of Minnesota, 1941.
10. Dukes, C. E. The classification of cancer of the rectum. J. Path. Bact., Lond., 1932, 35: 323–332.
11. Eker, Reidar. Carcinomas of the stomach; investigation of the lymphatic spread from gastric carcinomas after total and partial gastrectomy. Acta chir. scand., 1951, 101: 112–126.
12. Garlock, J. H. Radical surgical treatment for carcinoma of cardiac end of stomach. Surg. Gyn. Obst., 1942, 74: 555-560.
13. Jamieson, J. K., and Dobson, J. F. Lectures on the lymphatic system of the stomach. Lancet, Lond., 1907, 1: 1061–1066.
14. Lahey, F. H., and Marshall, S. F. Combining splenectomy with total gastrectomy. Surg. Gyn. Obst., 1941, 73: 341–344.
15. Lewis, F. J., and Wangensteen, O. H. Explorations following resection of the colon, rectum, or stomach for carcinoma with lymph node metastases. Surgical Forum, 1950; American College of Surgeons. Pp. 535–540. Philadelphia: W. B. Saunders Co., 1951.
16. McNeer, Gordon, Sunderland, D. A., McInnes, George, Vandenberg, H. J., Jr., and Lawrence, Walter, Jr. A more thorough operation for gastric cancer; anatomical basis and description of technique. Cancer, 1951, 4: 957–967.
17. ReMine, W. H., and Priestley, J. T. Late results after total gastrectomy. Surg. Gyn. Obst., 1952, 94: 519–525.
18. Rouvière, Henri. Anatomy of the Human Lymphatic System. Translated by M. J. Tobias. Ann Arbor: Edwards Brothers, Inc., 1938.
19. Sunderland, D. A., McNeer, Gordon, Ortega, L. G., and Pearce, L. S. The lymphatic spread of gastric cancer. Cancer, 1953, 6: 987–996.
20. Sweet, R. H. Total gastrectomy by the transthoracic approach. Ann. Surg., 1953, 138: 297–310.
21. Walters, Waltman, Gray, H. K., and Priestley, J. T. Carcinoma and other malignant lesions of the stomach. Philadelphia: W. B. Saunders Co., 1942.
22. Idem. Advances in the surgical treatment of cancer of stomach. Proc. Mayo Clin., 1952, 27: 156–161.

ASSOCIATED GASTRIC AND DUODENAL ULCERS

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SIR DAVID WILKIE was one of the first to remark upon the relative frequency with which duodenal ulcers and gastric ulcers may occur together in the same subjects, when in 1926 he reported that in a series of 300 patients upon whom he had operated for peptic ulcers he had found combined ulcers in 42, 1 in 6 of the patients with duodenal ulcer also having a gastric ulcer, and more than half the gastric ulcers being associated with duodenal ones.

However, this does not appear to be a true picture of the incidence of concomitance, for 3 years later Hurst and Stewart reported on 4,000 postmortem examinations in the course of which they had found 173 chronic gastric and 230 chronic duodenal ulcers, but only 21 cases in which these lesions were combined, 5.5 per cent, as against Wilkie's 14 per cent. Nevertheless, if gastric ulcer and duodenal ulcer were in no way related, then on chance alone Hurst and Stewart could have expected only 10 cases of concomitant ulcers, and their actual discovery of 21 is statically of a high order of significance.

On the face of it, there is nothing remarkable in the observation that the presence of one peptic ulcer predisposes to the development of a second, for the many similarities between duodenal and gastric ulcers have led to a widespread belief that they have etiologic factors in common. However, as well as the similarities which exist between duodenal and gastric ulcers, there are also well marked differences between the types of people who are attacked by the two lesions. For, whereas duodenal ulcer develops on a basis of acid hypersecretion, hypertonicity, and rapid gastric evacuation, gastric ulcer is, in the main, associated with a normal or low rate of secretion and a stomach that is sagging, sluggish, and slowly emptying.

If there are etiologic factors common to both duodenal and gastric ulcers then presumably it is these other differing features which determine the site of the ulcer, and it might be expected that patients whose physical characteristics lay somewhere between the two extremes should occasionally develop both lesions. As will be seen, however, it is not patients of this kind who do indeed get combined ulcers.

It seemed to the writer, on the other hand, that so fundamental were the differences between gastric and duodenal ulcer subjects that the two lesions should have been mutually exclusive and that some new factor must have begun to operate before a gastric ulcer could complicate a duodenal ulcer or vice versa. Among 347 patients operated upon for peptic ulcers 32 had been encountered with a gastric as well as a duodenal lesion, and a factor common to them all was discovered to be that of gastric retention.

With the help of his colleagues, 103 more cases of concomitant gastric and duodenal ulcers were then collected on which to verify his findings and make further observations. At the same time an additional 16 cases were encountered in which other lesions obstructing the gastric outlet had caused retention and in which gastric ulcers had developed. Of the whole series of 135 subjects discovered or confirmed at operation to have, or to have had, both duodenal and gastric ulcers, 111 were men and 24 were women, of ages ranging from 26 to 84 and averaging 53 years. All but a few of these patients had long histories of dyspepsia, and the average age of this group at the onset of their symptoms was approximately 30 years.

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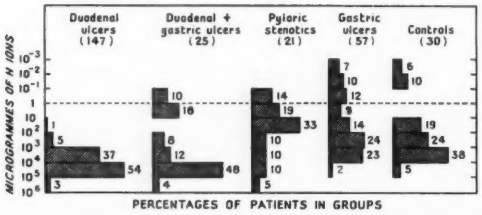

FIG. 1. Micrograms of ionized hydrogen in whole of gastric night secretion. The figures for the concomitant ulcer group are seen to lie between those for duodenal ulcer and for pyloric stenosis. (From Johnson, H. D. *Lancet*, Lond., 1955, 1: 266.)

THE ORDER OF APPEARANCE OF THE LESIONS

In 30 cases both ulcers were discovered when roentgenograms were first taken. In 7 neither ulcer was ever detected by radiography but both were present at operation. Of the remaining 98 patients, 21 had been operated on for acute perforations of peptic ulcers, all of them duodenal, some time before a gastric ulcer was discovered as well. In 70 cases, the patient had been treated for a number of years for a duodenal ulcer confirmed radiologically before roentgenograms or operation also revealed a gastric ulcer. In only 7 cases was a gastric ulcer seen first. In all these, the duodenal ulcer escaped detection altogether at radiologic examination and presented as a healed scar at operation, therefore, there was no reason to suppose that it had not actually preceded the gastric ulcer in these cases too, as it apparently had in all the other 91.

Having observed that, in cases of combined duodenal and gastric ulcers, it was usually, if not always, the duodenal ulcer which appeared first, we should expect to find that combined ulcers occurred in subjects of the duodenal ulcer rather than the gastric ulcer type. This is indeed so and was confirmed by investigations of gastric secretion.

TABLE I.— FINDINGS AT OPERATION IN 135 CASES

Duodenal ulcer	*Gastric ulcer*	*No.*	*Per cent*
Healed	Healed	4	3
Active	Healed	7	5
Active	Active	32	24
Healed	Active	92	68
Stenosis	Active	39	29
Stenosis	Healed	1	1

SECRETION PATTERN

Thirty-two patients with combined ulcers were subjected to all night secretion tests, and the results are shown in Figure 1, compared with those obtained from similar tests in 147 cases of duodenal ulcer, 57 cases of gastric ulcer, 21 cases of pyloric stenosis, and 30 patients without dyspepsia. The mass of ionized hydrogen in the whole of the bulked gastric night secretion has been calculated from its volume and hydrogen ion concentration. Fifty-seven per cent of the duodenal ulcer subjects and 52 per cent of combined ulcer subjects produced over 10 milligrams, but only 2 per cent of those who had gastric ulcers alone. Associated ulcers are thus clearly shown to occur in patients of the hypersecreting, duodenal ulcer type, rather than in the hyposecreting, gastric ulcer type.

GASTRIC RETENTION

Well marked pyloric stenosis with a distended, retentive stomach having been a feature of several of my own earlier cases of combined ulcers, this was specially looked for in subsequent cases. It then soon became evident that an unusual degree of gastric retention was almost the rule when combined ulcers were present. When evidence of gastric retention was sought in the records of the other patients making up the larger series, stenosis was found to have been mentioned in the operation notes in 33 per cent and reported by the radiologist in a further 22 per cent. Among the remainder, there was clinical evidence of gastric retention such as succussion splash or copious vomiting, in another 9 per cent, making in all some 64 per cent in whom evidence of gastric retention had been reported. Of the remaining 36 per cent it can only be said that, if pyloric obstruction was present, evidence of it was not recorded in the notes.

Comparison of the distribution patterns in Figure 1 show that the mass of hydrogen ions in the continuously aspirated all night

gastric secretions of duodenal ulcer subjects undergoes a remarkable reduction as pyloric stenosis becomes established. It has often been stated in the past that acidity falls because retention causes gastritis which destroys the secreting capacity of the stomach. This is not so, however, for actually when continuous aspiration is used the volumes of secretion obtained from patients with pyloric stenosis are often enormous. It is more probable that the disappearance of "free hydrochloric acid" is due to enhanced intragastric buffering, the abundant acid secretion being therefore now only reflected in the high level of "total acid" so often seen in these patients.

Though gastric retention has been claimed to be a usual feature of patients with combined ulcers, it is seen from Figure 1 that only a few of these patients exhibit the marked buffering found in the majority of those with stenosis but no gastric ulcers. This observation suggests that it is those patients with pyloric stenosis who do not develop or have not yet developed marked introgastric buffering who are liable to gastric ulcers.

Examination of the records of a continuous series of 331 patients admitted to hospital for pyloric stenosis showed that 52 (16 per cent) of them were later discovered also to have gastric ulcers. Ten of these could not be seen at x-ray examination; indeed, gastric ulcers are notoriously difficult to detect radiologically in the presence of gastric retention. These 10 came to light at operation or in the postmortem room.

OPERATIVE FINDINGS

The most frequent finding at operation was of a healed stenosed duodenal lesion and an active, often huge, and sometimes bleeding gastric ulcer. Only 8 per cent of the gastric ulcers were healed, whereas 70 per cent of the duodenal ulcers were inactive and scarred. Both ulcers were active in 22 per cent and both healed in 3 per cent. Antral gastritis is a common accompaniment of duodenal ulcer, but when pyloric stenosis is present, the inflammation may be very severe (Fig. 2).

FIG. 2. A gastrectomy specimen from a patient with a large gastric ulcer associated with an active duodenal ulcer (not seen in the specimen) and pyloric stenosis. The specimen shows marked antral gastritis, congestion, and edema obliterating the rugal folds of the prepyloric half of the specimen.

OTHER CAUSES OF GASTRIC RETENTION

Sixteen additional cases illustrate how gastric retention due to other causes than duodenal ulcer may be complicated by gastric ulcer.

In 3 cases, the gastric ulcer was associated with adult hypertrophic pyloric stenosis; an extreme instance is shown in Figure 3.

In 6 patients, gastroenterostomies had been earlier performed for duodenal ulcers, and later the development of gastric ulcers had occasioned further surgery. Three of them were found to have active jejunal ulcers as well, and the other 3 had the scars of anastomotic ulcers and stomal stenosis with gastric retention. Another patient who had had a gastroenterostomy for duodenal ulcer later had this undone. In due course he developed a huge gastric ulcer which bled 15 times. On the fifteenth occasion, emergency gastrectomy was performed and pyloric stenosis was discovered.

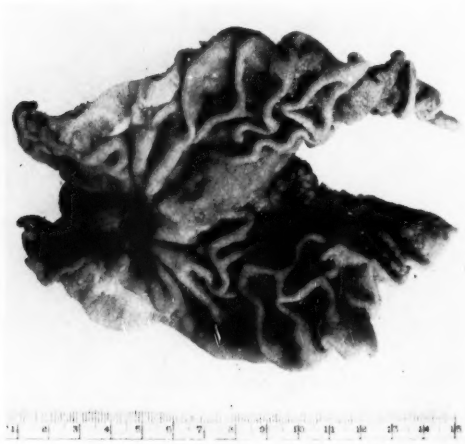

FIG. 3. An example of gross pyloric hypertrophy in an adult, associated with a chronic gastric ulcer. The muscle of the prepyloric antrum is more than a centimeter thick. (The stenosis which was present is no longer in evidence after opening and fixing of the specimen.)

Having already begun to suspect that pyloric stenosis might cause a gastric ulcer and having observed the prolonged gastric retention which often followed vagotomy, I wrote in 1947: "It may well be that gastric ulcer will prove to be one of the late complications of vagotomy in man" (2).

Since that melancholy prediction a number of such ulcers following vagotomy alone have been reported and 5 have come within my own experience (Fig. 4). All 5 patients had healed duodenal ulcers with much scarring and gross delay in gastric emptying.

FIG. 4. A gastrectomy specimen, showing a giant gastric ulcer which developed 2 years after vagotomy for a duodenal ulcer. Pyloric stenosis is also present. (This specimen has been turned inside out instead of being split open.)

One patient has been discovered who had a carcinoma obstructing the pylorus and a big simple ulcer proximal to it.

The last patient, though he did not have a localized chronic gastric ulcer, illustrates the great severity of the erosive process which may occur in the presence of pyloric obstruction. The patient was admitted to the hospital with hematemesis. Continued massive hemorrhage finally demanded surgery and he was found to have arterial bleeding from a large and very inflamed duodenal ulcer. The stomach was hugely distended and some 3 inches thick with edema. Gastrectomy was performed and during the making of the anastomosis there was extruded from the gastric stump what proved to be a slough of almost its entire mucosal lining. The gastrectomy specimen is shown in Figure 5. (The patient recovered.)

HEMORRHAGE IN COMBINED ULCERS

When a gastric ulcer develops as a complication of gastric retention it does not behave as other gastric ulcers do but tends to become very large and deep and resistant to treatment. It is also particularly prone to massive hemorrhage. Of the gastric ulcer patients admitted to the hospitals from which this series is drawn, 8 per cent had bled at some time, but of the patients with both duodenal and gastric ulcers, 47 per cent had had hemorrhages and 20 per cent had had several.

Thirteen patients of the series were admitted actively bleeding and underwent emergency gastrectomies. In every case it was the gastric ulcer which was bleeding, and this would be expected since the gastric ulcer is nearly always active and the concomitant duodenal one usually healed.

In 2 patients with stenosed, healed duodenal ulcers, hemorrhage was coming from several of numerous acute gastric ulcers. It is

important to have this possibility in mind when operating for hematemesis on patients with duodenal ulcers. Indeed, if a duodenal ulcer is encountered when performing an emergency laparotomy for gastrointestinal hemorrhage, a very thorough search should be made for the concomitant gastric ulcer which is often the source of the blood in these cases. Such ulcers may be impalpable from outside the stomach, as were those in the case illustrated in Figure 6.

FIG. 5. A gastrectomy specimen showing severe gangrenous gastritis. This stomach was removed at an emergency operation for massive bleeding from a duodenal ulcer with marked pyloric stenosis. Most of the mucosa from the fundus and a large part of the body of the stomach has sloughed. The stomach was more than 2 inches thick with edema.

TREATMENT

When a gastric ulcer is present alone and there is no evidence of acid hypersecretion, I hold that there is no purpose in resecting more than the minimum of stomach consistent with the removal of all diseased tissue, and it is my own practice to divide the stomach in a sigmoid fashion as described in a previous article (4) so as to conserve more of the healthy greater curvature. I have had no case of recurrent ulcer after 120 such operations for gastric ulcer in which often no more than half the stomach was removed.

Sleeve resections for gastric ulcer were a failure, however, and I suggest that this was because they resulted in denervation of the distal segment, and therefore caused gastric retention and recurrent gastric ulcers.

The surgical treatment of duodenal ulcer presents an altogether different problem, for the operation must include among its aims the control of acid hypersecretion. When both gastric and duodenal ulcers are present it is important to remember that it is an operation suitable for the hypersecreting duodenal ulcer patient which is required, and that the moderate resection recommended for gastric ulcer alone would be inadequate. As an alternative to radical gastric resection, more limited resection may be combined with vagotomy. Two hundred sixty five patients with duodenal ulcers or combined duodenal and gastric ulcers so treated have been followed 1 to 7 years without recurrence (4).

The Billroth I operation for gastric ulcer occasionally results, inadvertently, in an excessively small stoma and gastric retention. It may well be the present increasing popularity of this usually excellent procedure will bring in its train a crop of recurrent gastric ulcers among those who develop such retention.

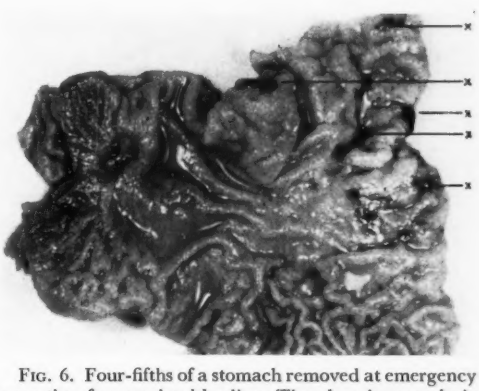

FIG. 6. Four-fifths of a stomach removed at emergency operation for massive bleeding. The chronic prepyloric ulcer had not bled but had produced pyloric obstruction. Hemorrhage came from a number of acute gastric ulcers (*x*), several of which can be seen to be filled with blood clot.

SUMMARY

Among peptic ulcer patients who come to postmortem examination some 5 per cent are found to have evidence of past or present ulceration of both stomach and duodenum. This is twice as many as might have been expected on chance alone. The proportion is higher still among those with more severe lesions and surgeons may encounter concomitant ulcers or their scars in some 10 per cent of patients subjected to gastrectomy.

An analysis of 130 cases of associated duodenal and gastric ulcers showed that those in which one ulcer was detected before the other, certainly in 93 per cent and possibly in all of them, the duodenal ulcer appeared first.

The patients were of the hypersecreting duodenal ulcer type rather than the hyposecreting hypomotile gastric ulcer type.

In 64 per cent there was definite evidence of pyloric stenosis and gastric retention, and it is suggested that this is an etiologic factor in the development of the associated gastric ulcers.

The gastric ulcers were large and prone to bleed and were more resistant to medical treatment than gastric ulcers not associated with duodenal lesions.

It was found that patients admitted to the hospital with pyloric stenosis are commonly later discovered to have gastric ulcers as well.

The implications of these findings are discussed and their bearing on treatment considered.

REFERENCES

1. Hurst, A. F., and Stewart, M. J. Gastric and Duodenal Ulcer. P. 97. New York and London: Oxford University Press, 1929.
2. Johnson, H. D. Vagotomy; present position. Postgrad. M. J., Lond., 1948, 24: 193.
3. Idem. The special significance of concomitant gastric and duodenal ulcers. Lancet, Lond., 1955, 1: 266.
4. Johnson, H. D., and Orr, I. M. Selective surgery for peptic ulcer. Surg. Gyn. Obst., 1954, 98: 425.
5. Wilkie, D. P. D. Coincident duodenal and gastric ulcer. Brit. M. J., 1926, 2: 469.

PARIETAL PLEURECTOMY FOR RECURRENT SPONTANEOUS PNEUMOTHORAX

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SPONTANEOUS PNEUMOTHORAX in apparently healthy individuals or "pneumothorax simplex" is a relatively common occurrence. It is almost always due to rupture of a subpleural air vesicle, occurs most often in young people and is 5 times more common in males. Indeed, it has been said by Schneider and Reissman that 1 of every 500 young men selected at random can present a documented history of spontaneous pneumothorax. Therefore, physicians working in schools and military establishments have been most impressed by the frequency of this accident, its often disabling character, and its numerous complications. Among young men "idiopathic" spontaneous pneumothorax is responsible for 1 of every 1,000 hospital admissions, and data from this hospital support previous reports: A discharge diagnosis of spontaneous pneumothorax appears 67 times among the first 71,606 hospital records, or 1 per 1,069 admissions.

In the military establishment spontaneous pneumothorax presents certain special problems. Air evacuation to treatment centers is often delayed because of lack of pressurized cabins. Hospitalization is usually prolonged because facilities for limited activity and ambulatory care are not provided. Return to duty is not the rule even after prompt and uncomplicated re-expansion. Even during the last World War when pressure in this regard was greater than now, less than 70 per cent of patients with a single episode of spontaneous pneumothorax returned to duty. The loss is more serious in flying personnel since highly trained individuals are involved and present regulations prohibit flying after a single episode of pneumothorax. Occasional return to flight status after adequate treatment has been reported by Paul and associates, but at least during the last war 36 of 41 pilots with spontaneous pneumothorax in the Army Air Training Command were permanently grounded, as reported by Leach.

The present treatment of spontaneous pneumothorax and its complications is fairly well defined. With a first episode and a small air space treatment is usually "conservative." For pneumothorax over 25 to 50 per cent catheter drainage with water trap decompression is advocated as safer and more effective than needle aspiration; tube drainage does not lead to complications other than slight temperature elevation and the re-expansion time is reduced from weeks or months to minutes or hours. Ambulatory treatment is now more common because of the increasing cost of hospitalization but has not been advocated in print. After re-expansion immediate return to ordinary activity appears logical because the onset of pneumothorax is only rarely occasioned by strenuous activity or unusual exertion and bears no relationship to type of occupation.

Tension and bilateral pneumothorax, two often fatal complications, require immediate catheter drainage with water trap decompression. Bilateral pneumothorax is more common than generally appreciated and occurs in 10 to 12 per cent of patients with spontaneous pneumothorax. Until recently it was fatal in approximately half of the cases.

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Spontaneous hemopneumothorax may carry a mortality of 20 per cent. It demands frequent aspiration with prompt replacement of blood and often thoracotomy with ligation of the source of bleeding, usually a torn vascular adhesion.

Chronic pneumothorax is established when re-expansion has failed to occur after some weeks of active therapy. This condition may persist without complications and with only moderate disability for many years, yet the ever present dangers of empyema or contralateral pneumothorax and the basic principle of optimal restoration of function are sufficient indications for vigorous efforts directed at re-expansion. Chronicity is usually due to: (1) adhesions under tension at the base of a torn bleb; (2) an epithelialized bronchopleural fistula in an area of scarring; (3) rupture of a congenital cyst with a large bronchial communication; and (4) collapse maintained by an imprisoning pleural cortex.

Induction of chemical pleuritis for the treatment of chronic pneumothorax was first suggested by Spengler because patients who contracted active pleuritis with effusion sometimes showed expansion of a previously collapsed lung. Poor results with irritating agents are borne out by the huge number of substances which have been suggested, and only 9 successful cases which have been reported over a 50 year period. Injection of irritating chemicals can lead to return of adequate function only if it is followed by closure of the fistula and immediate apposition of pleural surfaces. Otherwise eventual obliteration of the air space will be due to pleural thickening, mediastinal shift, chronic accumulation of fluid, and eventual fibrothorax.

"Closed" surgical procedures, advocated in the treatment of chronic pneumothorax, including thoracoscopy with lysis, phrenic paralysis, and closed drainage with forceful suction have succeeded at times if adhesions under tension were responsible for failure of the rent in the lung to close. Healing of bronchopleural fistulas has been reported by Waterman after cauterization under thoracoscopic vision. Insufflation or local application of caustic substances under thoracoscopic control has been advocated, but apparently only Brock has used this method with any degree of success.

Open thoracotomy with inspection of the defect, lysis of adhesions, closure or excision of the bronchopleural fistula, or decortication of the bound down lung were first suggested between 1937 and 1947. An increasing number of reports during the past 7 years of uniform success with the direct surgical approach with low mortality and brief hospitalization appear to justify the general acceptance of exploratory thoracotomy for chronic spontaneous pneumothorax.

Recurrence, the most common complication of spontaneous pneumothorax, has been reported in 15 to 42 per cent of recent large series. Of 1,080 carefully documented cases collected from the literature since 1944, and not including presentations devoted to treatment of this complication, 245 patients or 22.7 per cent have had 1 or more recurrences. However, histories of "similar pain" or "pleurisy" have not been counted as previous episodes and follow-up has usually been limited to 1 or 2 years. Long range studies by Myers and by Perry on the other hand have brought to light first recurrences from 10 to 21 years after the initial episode, and the mean interval between first and second episodes was 3.1 years. Therefore, it is thought that recurrences are more frequent than heretofore believed, and Maxwell has said that in any given individual with spontaneous pneumothorax a recurrence is as likely to occur as not. Active measures aimed at prevention of recurrence are indicated especially if there has been more than 1 episode. The threat of tension or bilateral pneumothorax, chronic physical disability due to fear of recurrence, loss of time, and expense with repeated hospitalization and, in certain cases, recurrences in rapid succession have led to early attempts at preventative therapy.

Induction of artificial pleuritis appears to be a more fruitful approach here than in chronic pneumothorax because early apposition of visceral and parietal pleura is more likely to occur. There has been extensive laboratory and clinical trial of artificial pleurodesis because until 15 years ago anchoring of the remaining lobe of the lung was considered an important preliminary to successful lobectomy. Experimentally a vast number of substances ranging from tuberculin, killed bacteria, peptone and india ink to ether, rubber solutions, formaldehyde, gum arabic, and turpentine have been tried, but finally there was almost unanimous agreement that: (1) injection or insufflation of irritating substances is "useless, uncertain, or dangerous"; (2) adhesions, if formed, are stringy, patchlike or filmy; and (3) thickening and fixation usually take place on the diaphragmatic and mediastinal pleura where they are least desirable. Substances used in the clinical treatment of recurrent spontaneous pneumothorax include: mild irritants which do not cause loss of substance such as iodized oil, dextrose, gomenol, and human blood; caustics like silver nitrate which cause tissue destruction; and physical irritants including various kinds of talc and kaolin. Further recurrences have been prevented particularly with use of the more irritating and destructive substances, but these reports are difficult to evaluate because they were, for the most part, confined to a single or a few cases, follow-up was limited to a year or less, and the number of failures has exceeded the number of good results.

Thoracoscopy and thoracotomy in recurrent spontaneous pneumothorax have demonstrated a cause for the condition in 90 per cent of cases so examined. Therefore, exploratory thoracotomy is now advocated with the aim of complete removal of the offending lesion. Local removal of subpleural blebs, bullae, valve vesicles or scar tissue, wedge excision, or segmental resection of the area bearing the lesion has been possible in most instances; plication of blebs or resection of the cyst wall and closure of the bronchial communication have been reported; lobectomy was rarely necessary.

In the majority of patients, the findings were such that the choice of operative procedure presented no problem. However, in three types of cases definitive treatment has not been possible. The first includes the considerable number of patients in whom the entire lung surface was apparently normal and no lesions or air leaks could be found; in the second group such a large part of the lung surface was covered with blebs that, in the interest of preservation of function, excision or plication could not be performed; the third and very small group comprises those poorly understood conditions in which the lung shows small cracks with demonstrable bronchopleural communications but without visible scars or vesicles. In these cases, definitive treatment has not been possible, and local application of irritants was the only applicable method. This has led to some good results, particularly in 25 patients of Brock who were treated by painting of the involved pleura with 20 per cent silver nitrate followed by later injections of less concentrated solutions. Selective application of tincture of iodine, insufflation of talcum powder under direct vision, and scrubbing of the pleural surfaces with rough gauze have also been advocated when no lesions were found or when blebs were too numerous for excision.

Pleurodesis is not definitive treatment and, with few exceptions, it has been used in recent years only when more direct approach was not possible. Recurrences have been reported even after use of the more violent irritants including silver nitrate, 67 per cent glucose, and talcum powder. It has been possible to induce artificial pneumothorax after several silver nitrate injections and failure has been recorded after as many as 20 talcum treatments. Pleurodesis has also lost favor because of pain which is often worse than that after major thoracotomy, febrile reactions, shock, the necessity for repeated treatments, and prolonged hospitalization which exceeds by far the period of recovery

TABLE I.—CLINICAL DATA AND OPERATIVE FINDINGS OF 7 MALE PATIENTS AFTER 9 OPERATIONS

Case	*Age, yrs.*	*No. prev. episodes Right*	*Left*	*No. days previous hospital*	*Previous treatment*	*Thoracoscopic and operative findings*	*Operations*	*Complications*	*Follow-up, months*
R.M.	22	0	4	93	None	Few large blebs, scars and broncho-pleural fistula at apex; many small blebs over entire upper lobe except lingular segment; multiple adhesions	Parietal pleurectomy over upper lobe; apical wedge excision; lysis of adhesions	None	15
M.D.	17	0	2	68	None	Very many minute blebs covering all of left upper lobe except lingula; thin gray cortex over entire lung	Apical parietal pleurectomy; lysis and visceral pleural decortication	— 5 episodes spontaneous pneumothorax on unoperated upon side	15
M.D.	17	5	2*	117	None*	Entire right lung covered by blebs and vesicles of varying size; apical scars	Total parietal pleurectomy; apical wedge excision	None	1
S.J.	19	5	0	146	Needle Aspiration	Right upper and middle lobes covered by small subpleural blebs; air bubbles dissecting under cortex of lower lobe	Parietal pleurectomy over upper and middle lobes; visceral decortication	None	14
J.B.	23	3	0	112	Tube Drainage	Entire right upper lobe covered by ½ to 2 cm. blebs; adhesions and scars at apex	Upper parietal pleurectomy; wedge excision at apex	2 episodes spontaneous pneumothorax on unoperated upon side	14
J.B.	23	3*	2	42	Tube Drainage*	Innumerable blebs of varying size over entire left lung; apical scars	Total parietal pleurectomy; apical wedge excision	None	1
F.N.	20	5	0	145	None	Many blebs over right upper and posterior aspect of lower lobe; thin gray cortex and adhesions	Total parietal pleurectomy; lysis and visceral decortication	Hemothorax 2 days postop.; resolution with SK-SD.	10
A.G.	22	0	6	80	None	Left apical and posterior blebs; multiple adhesions	Lysis and total parietal pleurectomy	None	6
T.S.	22	2	0	101	None	3 large thick walled apical blebs; many small vesicles along fissures	Total parietal pleurectomy; apical wedge excision	None	3

*Pleurectomy performed previously on the opposite side.

after surgery. Further, use of powder has resulted in talcum embolism with hemiplegia both in man and experimental animals. Worst of all, the stipulated ideal of pleural fusion without formation of a restricting membrane has often not been attained. Severe pleural changes and fibrothorax have been seen at this and other hospitals after talcum poudrage and silver nitrate injection, and thick pleural membranes are apparent on published postoperative roentgenograms of others. Surgical removal of a pleural cortex due to talcum granuloma has proved extremely difficult. The loss of pulmonary function with fibrothorax is especially alarming because of the frequency of later spontaneous pneumothorax on the opposite side. Contralateral spontaneous pneumothorax has occurred shortly after surgery in at least 1 patient in every series dealing with surgery for recurrent or chronic pneumothorax including our own and has proved fatal when the original operation was extensive.

This report deals with a new technique for definitive surgical treatment of recurrent spontaneous pneumothorax for patients in whom local excision is not applicable either because resection of all the blebs would entail loss of an unjustifiably large amount of functioning lung tissue or because no lesions can be found on the lung surface.

MATERIAL AND METHODS

After bronchiectasis, recurrent spontaneous pneumothorax was the most common cause for admission to the thoracic surgery section, and, during the first 15 months of its operation, accounted for 11 per cent of all major thoracic procedures. Wedge and segmental resection or local excision of blebs was the rule. A search for a new definitive treatment was made when a patient (R. M.) was admitted in whom thoracoscopy revealed a left upper lobe entirely covered with subpleural blebs (Table 1). Resection of the involved area would have entailed excessive

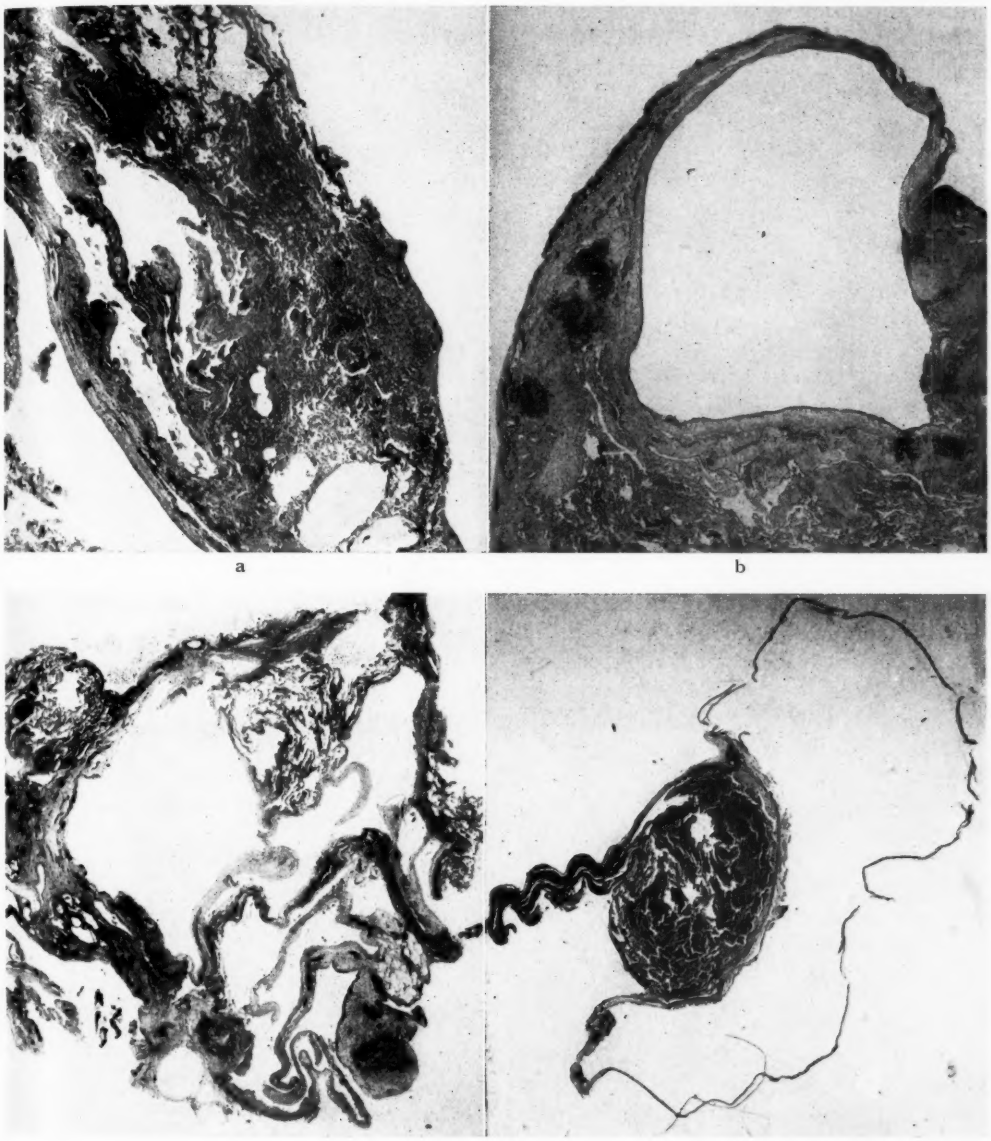

FIG. 1. Tissue sections from lung wedges removed at operation. a, Patient R. M. There are extensive areas of scarring and atelectasis in the region of the bronchopleural fistula, and intrapulmonary bullae and blebs under a greatly thickened pleura. b, Patient T. S. Scar tissue and chronic inflammatory reaction are seen immediately underneath the large bleb; there is pleural reaction and thickening. c and d, Sections are from patient J. B. c, The lesion removed from the apex of the right lung shows thickened pleura covering many blebs and much chronic inflammation. d, The section was excised as a biopsy specimen from the apex of the left lung. It was fixed with the Carmalt clamp in place to maintain inflation of the lesion. The bleb which was one of several hundred is covered by normal pleura. The lung tissue underneath shows mechanical compression due to clamping.

loss of lung tissue. Artificial pleurodesis seemed undesirable because of the prospect of prolonged treatment and observation in a patient who already had spent 93 days in the hospital with 3 recurrences in rapid succession. Also, there had been recurrences at this institution after talc poudrage.

It was thought that pneumothorax could recur only in the presence of a potential intrapleural space. Elimination of this space by removal of either pleura suggested itself as definitive and logical treatment. The visceral pleura forms an anatomic unit with the lung and cannot be removed without grave and permanent injury. The parietal pleura, however, is connected to the thoracic cage only by the endothoracic fascia, a layer of loose areolar tissue. The anatomy of this plane of cleavage was investigated in great detail when extrapleural pneumonolysis was developed for the treatment of pulmonary tuberculosis. Continued mobility and unimpaired functioning of the thoracic cage following dissection of the parietal pleura have been demonstrated. Dissection in this plane is often resorted to for pulmonary resection in the face of dense pleural symphysis or visceral pleural involvement by tumor and has made possible pneumonectomy in the presence of an infected pleural space.

Selection of patients. Only two criteria were used for parietal pleurectomy: first, a documented history of 2 or more episodes of spontaneous pneumothorax on the same side, and, second, a thoracoscopic or operative finding of extensive pleural involvement by blebs or vesicles. During 1954 seven patients were referred who fitted these criteria (Table I). Additional pleurectomies were performed when 2 of these patients (M. D. and J. B.) returned after repeated episodes of pneumothorax on the opposite side. All were young men and all had at least 2 and as many as 5 episodes on the same side documented by previous records and roentgenograms. Several patients also reported other episodes of sudden chest pain and dyspnea which had not been further investigated. Previous treatment had consisted of bed rest and search for underlying pulmonary disease. One patient (J. B.) with repeated tension pneumothorax had had catheter drainage on 2 occasions (Fig. 3), and another (S. J.) had a single needle aspiration. All patients were afebrile and asymptomatic when first seen on this service and none showed a reaction after intradermal injection of first and second strength P.P.D. In 2 patients who were referred from some distance, the lung had been allowed to expand prior to air evacuation; an air space was still present in the remainder.

Thoracoscopy. Taking the lead of others thoracoscopy was performed in every case. This simple procedure affords a good view of most of the lung surface and the information gained may lead to a more rational surgical approach. Indeed, the pathologic process was readily visualized in every case (Table I). In the first patient who had 3 recurrences in 6 weeks (R. M.) a bronchopleural fistula was seen in addition to many blebs. Multiple adhesions were seen in 3 instances usually at the base of large blebs. In 1 case (S. J.) thoracoscopy was misleading: Clusters of tiny blebs were seen over the entire lung surface. At operation only the upper lobe was found to be involved; small air bubbles had dissected underneath a thin, transparent cortex covering the lower lobe and this had given the appearance of blebs. A perfectly normal and airtight visceral pleura was seen in this region when the cortex was stripped away. It is suspected that the thoracoscopic picture described by Brock as "cuckoo spit" or "porous pleura" may have been simulated by air dissection of this kind. Following thoracoscopy a small catheter was introduced through the trocar shield and the tube sealed with a water trap. Deep breathing and coughing were encouraged until the lung was fully expanded and the catheter was then withdrawn (Figs. 2 to 4).

Operative procedure. Operation was delayed for at least 10 days to permit preoperative function studies with fully expanded lungs. Maximal preservation of the thoracic cage was an important consideration in selection

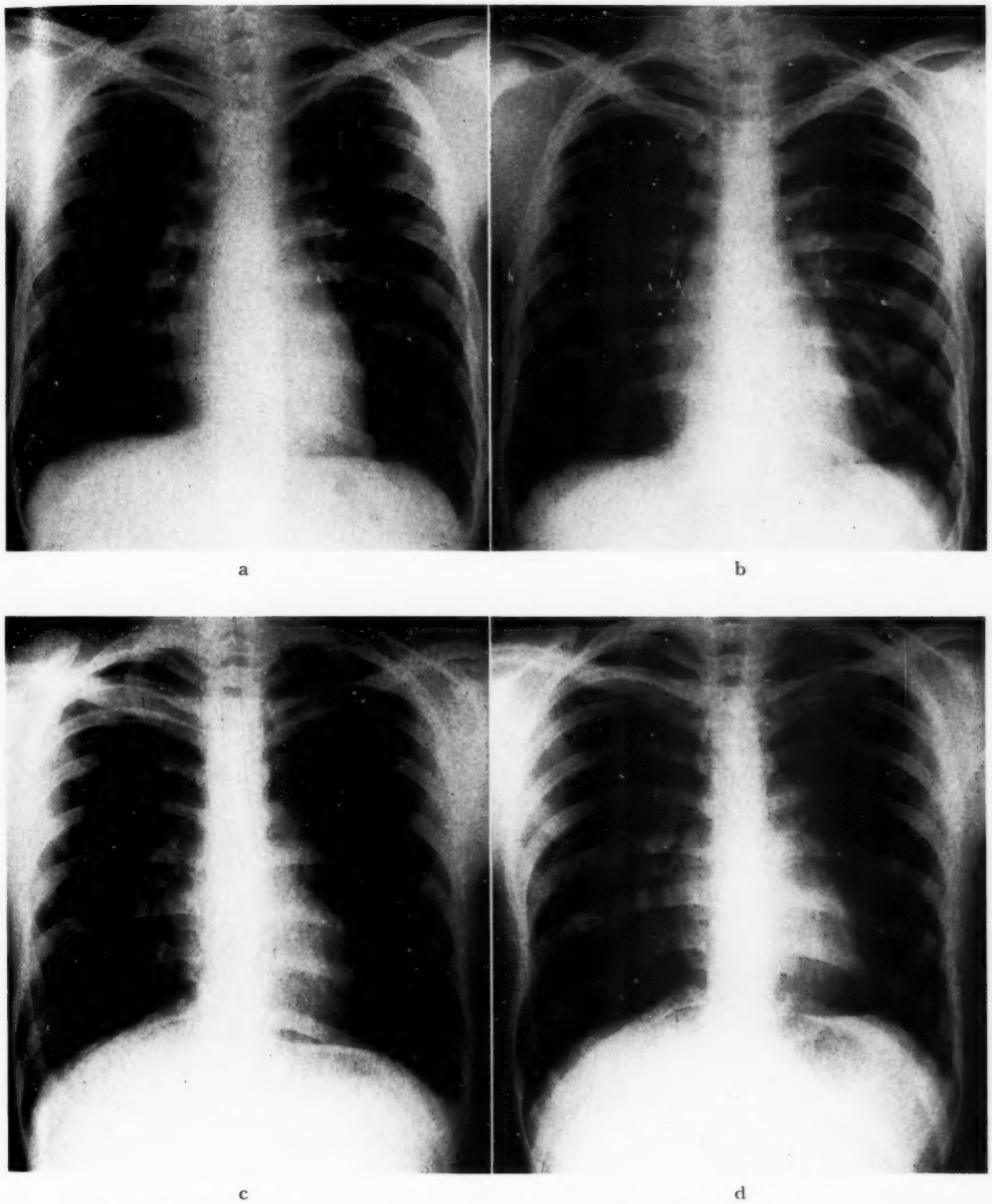

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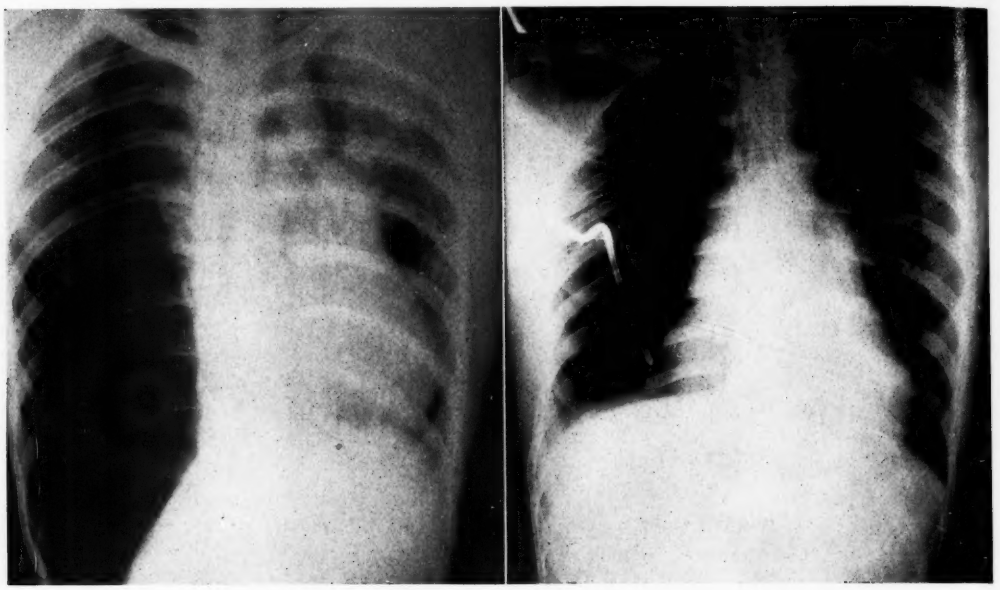
FIG. 2. Preoperative and postoperative chest roentgenograms. a, b, Patient R. M. a, One month before operation with both lungs fully expanded; b, 2 months after wedge resection and parietal pleurectomy over the left upper lobe. c, d, Patient M. D. c, One month before operation with both lungs expanded; d, 1 month after left upper parietal pleurectomy and visceral decortication. The costophrenic angles are clear and there is no evidence to be found of residual fluid or pleural thickening.



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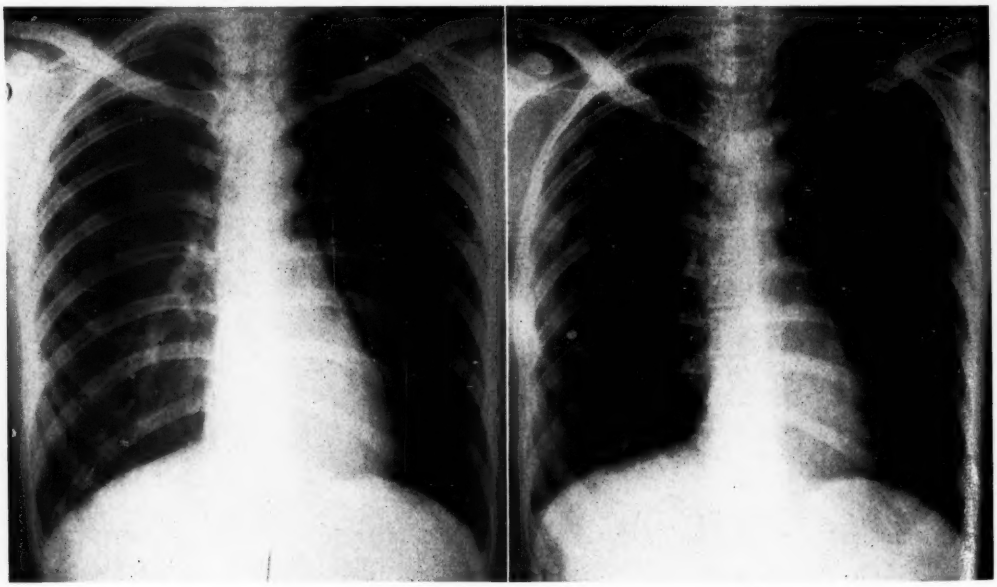
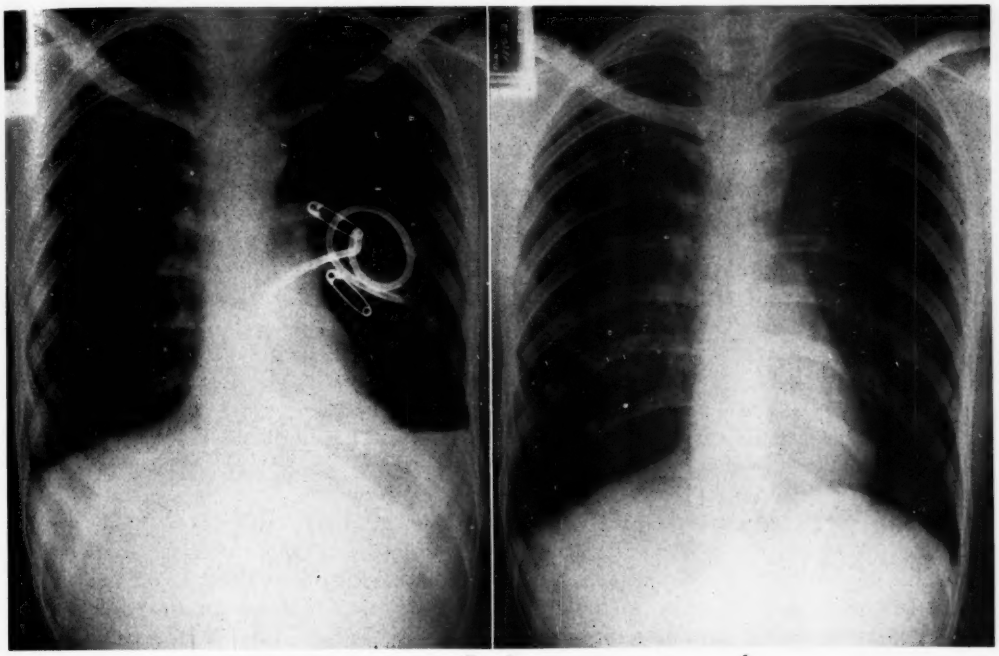


c d

FIG. 3. Chest roentgenograms of Patient J. B. a, Severe tension pneumothorax on the right 2 months before operation. b, Partial relief after intercostal drainage. c, Both lungs fully expanded 1 week before operation. d, Eleven days after right parietal pleurectomy and wedge excision of lung. e, Left spontaneous pneumothorax with intercostal drainage 4 months after operation on the opposite side. f, After bilateral total parietal pleurectomies and apical wedge resections.



e FIG. 3. f

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of the approach. A posterolateral intercostal incision was made in the fifth or sixth interspace. Adequate exposure was obtained with a child-size Tuffier retractor without interruption of ribs. An anterior incision in 1 case (A. G.) afforded less access to all aspects of the parietal pleura, airtight closure was more difficult, and there appeared to be more pain postoperatively.

Subpleural, thin walled, small vesicles and blebs were distributed quite extensively over the lung surface in all cases. The entire apical and posterior segments of the upper lobe were involved in 2 patients, the entire upper lobe except the lingular segment in 3, the upper lobe except the mediastinal aspect in 2, and the entire upper lobe and margins of middle and lower lobes bordering on the major and minor fissure in 1 case. In the patient with the most extensive involvement all the pleural surfaces of the lung except the mediastinal and diaphragmatic aspects were studded with small blebs.

In every case involvement was too extensive for local or wedge excision or for segmental extirpation. Application of positive pressure with the lung submerged in saline solution revealed a partly epithelialized bronchopleural fistula in 1 case (R. M.) Multiple adhesions were divided in 3 cases. In 5 patients there was, in addition to the generalized disease, an area of scarring at the very apex of the lung with larger, more thick walled blebs; in these instances this area was grasped between curved Carmalt clamps and a wedge including scar, large blebs, and, in 1 case, a bronchopleural fistula was excised (Fig. 1). The defect was closed in two layers with a continuous suture of fine chromic gut. A thin, gray, translucent cortex covered the entire lung of 3 patients but did not appear to limit full expansion. A similar but thicker layer has been a common finding in patients with chronic pneumothorax. In our cases the membrane was attributed to fibrin deposits following minimal pleural effusion

during previous episodes of collapse which could be demonstrated on old roentgenograms. In all 3 cases visceral decortication was performed without difficulty.

The rib retractor was then removed and the parietal pleura grasped with hemostats at the upper margin of the incision. Separation in the layer of areolar tissue was commenced with bronchoscopy wipes and continued by finger dissection when the flap was large enough. Less accessible areas were freed with moist gauze held in sponge-holding forceps. Care was taken to avoid inclusion of intercostal fat and neurovascular bundles which may be stripped down quite easily, particularly at the apex. In patients with upper lobe involvement, the parietal pleura in apposition to that lobe was resected and the mediastinal pleura was removed down to the arch of the aorta or azygos vein, but no special effort was made to remove small areas of pleura over the great vessels and nerves. In patients with more extensive involvement, the entire parietal pleura was resected except for the diaphragmatic surface and the mediastinum below the hilus. Usually the field was entirely dry; occasional capillary oozing from the denuded chest wall was controlled by application of warm, moist packs. Parietal pleurectomy required from 5 to 10 minutes and was somewhat easier in patients with a slightly thickened pleura.

The chest cavity was then washed with a large quantity of saline solution, and a careful search was made for injured intercostal vessels. One large urethral catheter was placed through a lateral stab wound and fixed in the posterior gutter; another was inserted below the axilla and fixed at the apex of the thoracic dome and both were connected to water trap bottles. Streptomycin and penicillin were introduced, the lung was expanded, the ribs reapproximated with pericostal chromic gut sutures, and the wound was closed in layers with interrupted silk.

Postoperative course and results. Prophylactic streptomycin and penicillin were given for 1 week. For sedation small doses of meperidine sufficed. Fluctuations of the water trap ceased in 24 hours and tubes were removed in 48 hours in all but 1 patient. Very little pleural reaction was observed; the lung was always fully expanded a few hours after operation and thoracentesis usually was not required (Figs. 2 to 4). All patients were out of bed the first day and entirely ambulatory on the fourth day. Breathing exercises and physiotherapy were started after 1 week and all patients were ready for duty 2 weeks after operation. Convalescent leave was given for administrative reasons and to allow for postoperative function studies.

Return to full duty including flying status in 2 cases was possible after 7 operations. One patient (R. M.) was seen by the physical evaluation board because his term of enlistment had expired. Another (J. B.) had a spontaneous pneumothorax on the opposite side 17 days after operation while on convalescent leave (Fig. 3). He experienced no unusual difficulty although collapse was estimated at 90 per cent, and he was treated with intercostal drainage at an installation near his home. During the next year he had 2 further episodes on the side not operated upon, and a second pleurectomy was performed 1 year later (Table I).

Complications. The postoperative course was uncomplicated after 8 procedures. One patient (F. N.) drained 1,200 cubic centimeters of fresh blood from the posterior tube during the second postoperative day, and the previously clear roentgenogram now revealed accumulation of fluid (Fig. 4). Two transfusions were given and the tubes were left in place for 5 days. After drainage had ceased and thoracentesis yielded only small clots, 200,000 units of streptokinase-streptodornase were injected and the tubes were withdrawn. Twenty-four hours later 1,400 cubic centimeters of hemolyzed blood were aspirated; the chest roentgenogram was clear after 1 further thoracentesis (Fig. 4).

Postoperative induction of pneumothorax. It was not anticipated that an opportunity

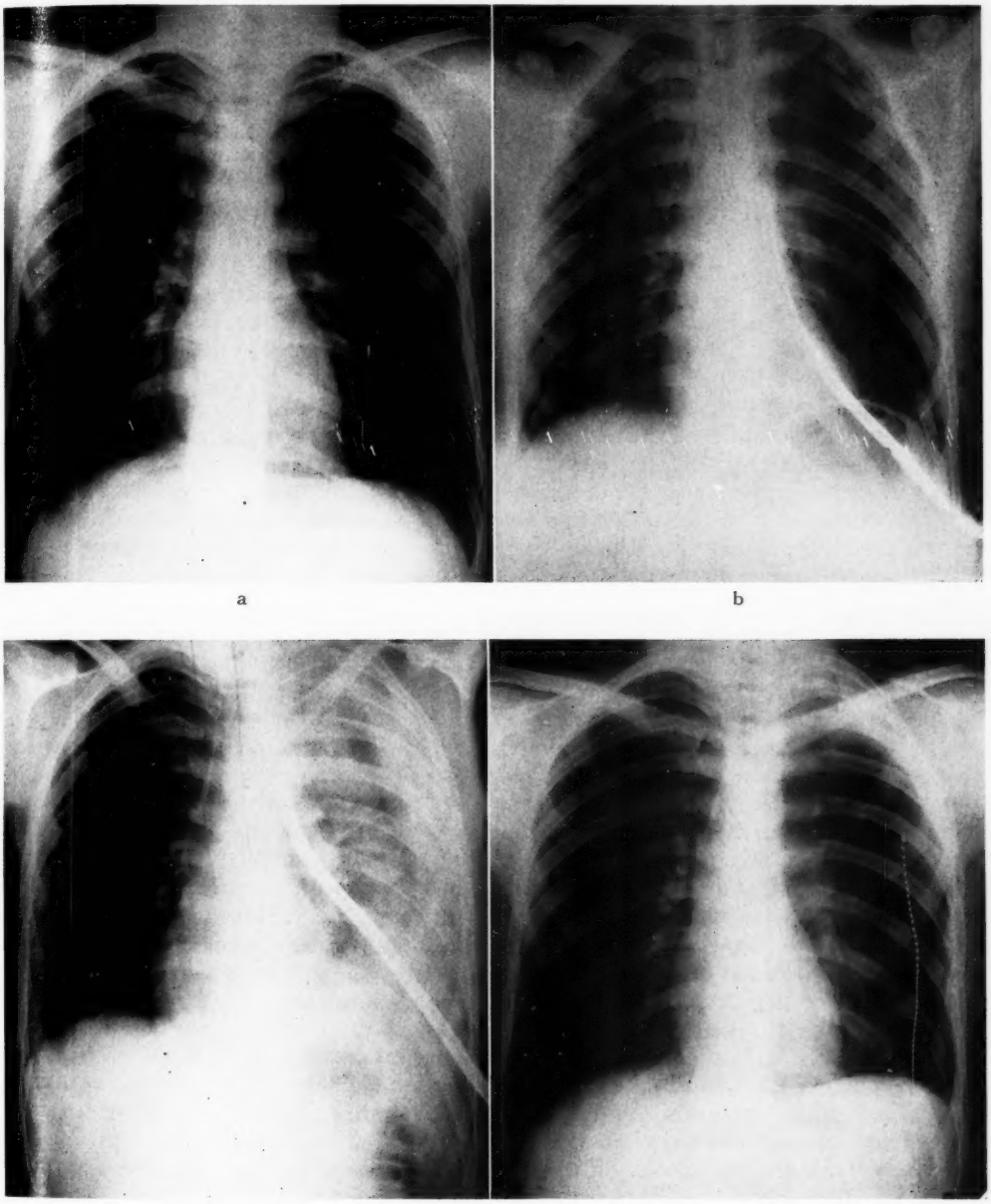

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FIG. 4. Chest roentgenograms of patient F. N. a, Four days before operation. b, Twenty-four hours after left total parietal pleurectomy and visceral decortication, there is little fluid and the lung is almost fully expanded at this time. The lower intercostal catheter is radio-opaque while the upper tube is not. c, Massive hemothorax and partial atelectasis 48 hours after operation. d, Discharge film 2 months after operation. After a single injection of streptokinase-streptodornase and multiple aspirations there is still pleural thickening at the apex and slight blunting of the left costophrenic angle.

TABLE II.—VITAL CAPACITIES OF 7 PATIENTS BEFORE AND AFTER 9 PLEURECTOMY OPERATIONS

	Preoperative		*Postoperative*		
Patient	*Liters*	*Per cent of predicted*	*Liters*	*Per cent of predicted*	*Per cent change*
R.M.	3.71	95	3.73	96	+1
M.D.	4.51	98	4.43	97	−2
M.D.	4.43*	97*	4.13	90	−7
S.J.	5.31	113	5.45	116	+3
J.B.	4.80	104	4.80	104	0
J.B.	4.80*	104*	4.41	96	−8
F.N.	4.40	102	4.15	97	−6
A.G.	4.20	94	4.15	93	−1
T.S.	4.21	93	3.86	85	−8
Mean	4.49	100	4.35	97	−3

*After unilateral and before bilateral pleurectomy.

would present itself in these patients to visualize the manner of symphysis between visceral pleura and chest wall. Therefore, an attempt was made after the last 5 operations to induce artificial pneumothorax to test the firmness of adhesion, a test which has not been reported previously to our knowledge. Exploratory thoracenteses were performed in these patients 17, 24, 29, 34, and 48 days after operation respectively. A 17 gauge blunt needle was introduced under local anesthesia in the eighth interspace in the posterior gutter, in the fifth interspace in the axilla, and in the second interspace in the midclavicular line. In 4 cases no fluid was obtained, no space could be found, and no pressure fluctuations were observed on the pneumothorax machine after injection of a few cubic centimeters of air under positive pressure in what was thought to be the correct plane. In 1 patient (S. J.) who had had pleural resection of the areas in apposition to the upper and middle lobes only no space was found anteriorly and in the axilla; posteriorly, pressure fluctuations were observed after injection of a little air, and 400 cubic centimeters of air were then introduced. Roentgenograms revealed complete fusion anteriorly and above the hilus of the lung; a small pneumothorax pocket was seen over the diaphragm laterally and posteriorly where pleurectomy had not been performed. The air disappeared spontaneously after 1 week.

Follow-up. A progress report was obtained from all patients including, in some cases, a note and roentgenograms from a medical installation in the vicinity. The periods of observation ranged from 15 months in 4 cases to 1 month in 2 cases (Table I). There were no recurrences on the side operated upon. All patients are entirely well, without complaints and performing their usual tasks which include flying in 2 cases and strenuous physical activity in 2 others.

Three patients (M. D., J. B., and A. G.) returned for re-evaluation and post-operative pulmonary function studies. Patient A. G. was entirely well 6 months after operation. Patient J. B., who suffered collapse of the opposite lung 17 days after operation, had another recurrence 6 months later on the side not operated upon which again required tube drainage (Fig. 3). Although the lung was fully expanded at the time of re-examination 14 months after the first procedure it was thought that the pleuropulmonary defect previously observed on the right side was probably bilateral. This was confirmed by exploration on the left and a parietal pleurectomy and wedge resection of apical scar tissue with several thick walled blebs were performed (Fig. 3). He returned to duty and has been well since.

Patient M. D. returned at our request for re-evaluation 15 months after operation. He reported that the lung on the side not operated upon had collapsed 5 times since leaving this hospital. This occurrence had led to a total hospitalization of 117 days, loss of flying status, and "transfer to a better climate." After this story was corroborated by records and roentgenograms from previous installations a right pleurectomy was performed (Table I). This patient also has been well since then (Fig. 2) and has returned to his former duties.

Pulmonary function studies. The vital capacity was the only available function test during the first year of observation. This test is inadequate in many respects. However, the possible functional impairment after parietal pleurectomy due to unexpanded lung or fibrothorax would result in a restrictive ventilatory insufficiency which is adequate-

ly reflected by diminution of vital capacity (2). Greatest importance was attached to assuring complete re-expansion after thoracoscopy and before preoperative evaluation of function because it is known that even a slight intrapleural pneumothorax may cause a considerable diminution of maximal ventilatory capacity. The best efforts of multiple determinations before surgery and 10 to 48 days after surgery are shown in Table II. The mean vital capacity for the group, which was 100 per cent of predicted before operation and 97 per cent afterwards, diminished by only 140 cubic centimeters. There was no correlation between postoperative diminution of vital capacity and extent of pleurectomy, performance of wedge resection, or decortication. The only obvious relationship was the time interval between operation and postoperative study. Patients who were studied 6 or more months after surgery (M. D. 1, J. B. 1, and A. G.) showed no loss of vital capacity while the 7 and 8 per cent losses (M. D. 2, J. B. 2, and J. S.) were recorded 2 to 4 weeks after operation.

More extensive ventilatory studies were completed in 4 patients before and early after operation (Fig. 5), and only late after operation in 4 patients (Table III). Our methods have been described in detail previously (2).

Results shown in Table III permit comparison of predicted normal function with results 2 to 15 months after pleurectomy. Spirometry at rest showed no abnormality other than a greater than basal oxygen uptake in 3 patients and slight hyperventilation demonstrated by a raised ventilation equivalent for oxygen in 1 patient. The vital capacity and its subdivisions were within 200 cubic centimeters of the predicted except in 1 patient in whom it was considerably less (T. S.). The maximal breathing capacity was larger than predicted in 2 patients and 82 per cent of predicted in 2 others. Timed vital capacities and air velocity indices revealed no obstructive ventilatory insufficiency. Bronchospirometry was the most important study in these patients and oxygen uptake the most significant of the 3 measurements made. If a normal share of function of the right lung is assumed to be 55 per cent of the total (5), the determined per cent of oxygen uptake of 54 and 57 per cent respectively of the 2 patients operated upon on the right side (T. S. and J. B.) suggests continued normal contribution to function after pleurectomy. Relative hyperventilation or unilateral diminution of vital capacity usually associated with restrictive pleural disease were not found. Split function studies after primary left operation (A. G. and M. D.) revealed an oxygen uptake on that side of 47 and 52 per cent which is a slightly larger contribution than the 45 per cent ordinarily expected from a left lung (Table III).

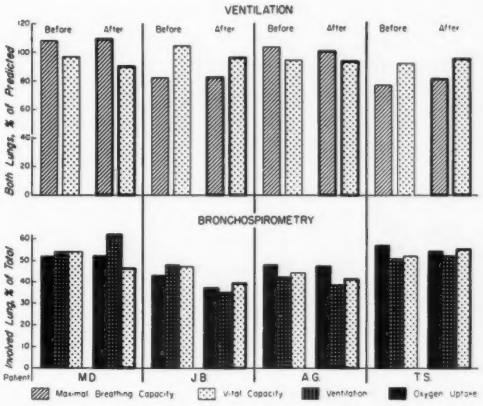

FIG. 5. Comparison of preoperative and early postoperative pulmonary function studies. Patients M. D. and J. B. were studied after unilateral and after bilateral pleurectomy and patients A. G. and T. S. before and after operation on one side.

More pertinent than comparison of postoperative findings with predicted values is comparison with preoperative findings because the rather large individual variations of "normal" performance are eliminated and there is no need to rely on prediction formulas with their large standard errors. Early postoperative results could be compared with preoperative data in 2 patients (A. G. and T. S.), and 2 others (M. D. and

J. B.) were studied after unilateral and early after bilateral pleurectomy (Fig. 5). No significant changes were observed in basal oxygen uptake, resting ventilation, or ventilation equivalent, and there was no tendency to hyperventilation after operation. Postoperative changes in vital capacity were at most 7 per cent in either direction, and the maximal breathing capacities were entirely unchanged in 2 cases and there was an insignificant increase in 2 (Fig. 5). The degree of shift in function based on change of oxygen uptake observed by bronchospirometry was within the limits of error of the technique in every case: In 2 cases the operations were on the right and oxygen uptake changed from 57 per cent of the total to 54 per cent in one (T. S.) and remained unchanged at 52 per cent in the other (M. D.). In J. B. who was operated upon on the left, the lung did assume a slightly smaller share of function which decreased from 43 to 37 per cent.

The only definitely abnormal physiologic findings early after operation consisted of slight diminution of lung volumes. That this was due to pain, weakness, and limitation of voluntary effort rather than to actual intrathoracic changes is suggested by the facts that lung volumes measured in the upright position were less altered, that the maximal breathing capacities remained unchanged, that late postoperative studies failed to show persistence of this defect, and that there was no accompanying asymmetry of function as determined by bronchospirometry.

DISCUSSION

Four complications were considered as possible sequelae during the planning of this operation: hemothorax, formation of a membrane in place of the parietal pleura, Horner's syndrome, and development of fibrothorax with loss of pulmonary function.

Hemothorax was feared as a complication because bleeding from a large denuded surface on the thoracic wall and superior mediastinum is often difficult to control following other extrapleural procedures. In our patients, unlike those with tuberculosis, empyema, or tumor, there was only a capillary blood supply to the parietal pleura and active hemostasis proved unnecessary. In the 1 patient in whom postoperative bleeding did occur (F. N.) an intercostal vessel was almost certainly torn when a neurovascular bundle was inadvertently pulled from the thoracic wall by blunt dissection at the apex. In retrospect, hemothorax should not be a problem after this procedure if the thoracic cavity is carefully inspected before closure.

A membrane may form on the denuded chest wall if immediate expansion of the lung fails to occur or is prevented on purpose. Such a smooth, glistening surface, indistinguishable from parietal pleura, has often been observed on a previously depleuralized chest wall when an established extrapleural pneumothorax was opened for conversion to modified thoracoplasty (14). This may give rise to another potential space and possible recurrence of air pockets. It was believed that these membranes had formed in the prolonged presence of air. Therefore, tubes with water traps were used in every case to promote immediate contact between visceral pleura and denuded chest wall, firm union, and ingrowth of the readily available blood supply. Drainage for 24 hours was the only measure necessary in our series. More active treatment including chest tube suction, endotracheal stimulation to promote cough, and even bronchoscopy might be indicated if complete re-expansion does not occur immediately. Unsuccessful attempts at induction of artificial pneumothorax and absence of recurrences suggest that membrane formation and development of a new potential space was not a problem in our patients.

A Horner's syndrome has been found after 39 per cent of all operations when extensive apical extrapleural dissection was necessary in the presence of empyema and thickened pleura. This complication has not been common after extrapleural dissection where lesions were confined to the pulmonary parenchyma (4). Nevertheless, with

TABLE III.—PREDICTED NORMAL VALUES AND RESULTS OF LATE POSTOPERATIVE PULMONARY FUNCTION STUDIES

	Patient M.D.		Patient J.B		Patient A.G.		Patient T.S.	
Examination	*Predicted*	*15 mos. postop.*	*Predicted*	*14 mos. postop.*	*Predicted*	*2 mos. postop.*	*Predicted*	*6 mos. postop.*
Height, in.	—	70.5	—	72.5	—	70	—	71.5
Weight, lbs.	—	144	—	127	—	141	—	176
Body surface, m^2	—	1.82	—	1.75	—	1.84	—	2.00
Oxygen uptake, c.c./min./m^2 B.S.	—	275	—	296	—	245	—	157
Ventilation, c.c./min./m^2 B.S.	—	5,240	—	5,530	—	7,370	—	4,100
Vent. equivalent, L./100 c.c. O_2	2.5	1.9	2.5	1.9	2.5	3.0	2.5	2.6
Respiratory rate	—	15	—	14	—	18	—	11
Inspiratory capacity, c.c.	3,430	3,305	3,460	3,160	3,360	2,970	3,410	2,450
Expiratory reserve, c.c.	1,150	1,080	1,150	1,280	1,120	1,060	1,140	680
Supine vital capacity, c.c.	4,580	4,385	4,610	4,440	4,480	4,030	4,550	3,130
Maximal breathing capacity, L./min.	141	152	130	107	138	138	150	122
Upright vital capacity, c.c.	4,580	4,430	4,610	4,800	4,480	4,150	4,550	3,860
Per cent exhaled, first second	70+	84	70+	84	70+	94	70+	87
first 2 seconds	85+	99	85+	97	85+	97	85+	92
first 3 seconds	95+	100	95+	100	95+	98	95+	98
Air velocity index	1.0	1.1	1.0	0.8	1.0	1.1	1.0	1.0
Bronchospirometry, per cent contribution of operated upon side: 1) O_2 uptake	55	52	55	57	45	47	55	54
2) Ventilation	55	54	55	52	45	38	55	52
3) Vital capacity	55	54	55	53	45	41	55	55

this complication in mind, special care was taken during dissection of the apical mediastinal pleura in our cases.

Pulmonary insufficiency does not always follow uncomplicated symphysis of the pleural surfaces. Many patients with normal pulmonary function at operation prove to have dense pleural adhesions which prevent the gliding action of the two pleural surfaces. Indeed, it has been pointed out that several mammals do not have pleural spaces. On the other hand, it is well known that pleural disease may be followed by severe restriction of ventilatory capacity, marked hyperventilation, and increased pulmonary arterial resistance. From the physiologic standpoint there appears to be a distinct difference between the effect of pleural thickening and fibrothorax following chronic empyema, chemical pleuritis, chronic effusion or poor re-expansion after pneumothorax, and the type of symphysis which follows a transient or mild acute inflammatory process. In our patients obliteration of the costophrenic angle, minimal pleural effusion, and limitation of motion of the involved chest wall all disappeared during the first 2 or 3 weeks after operation (Figs. 2 to 4). Breathing exercises, physiotherapy, and ward duties may have accelerated this process. At the time of discharge all chest roentgenograms appeared essentially normal, and there was no evidence of impaired thoracic or diaphragmatic motion by fluoroscopic and physical examination. Pulmonary function studies revealed a moderate restriction of lung volumes early after operation (Fig. 5) but other tests, including resting spirometry, timed vital capacity, maximal breathing capacity, and bronchospirometric determination of oxygen uptake, ventilation and vital capacity of each lung separately, remained within normal limits or were unaltered by surgery. Follow-up physiologic studies up to 15 months after operation failed to demonstrate any of the criteria usually associated with restrictive pulmonary insufficiency due to chronic pleural reaction and fibrothorax: there was no hyperventilation at rest or during exercise and no severe diminution of vital capacity with moderate decrease of maximal breathing capacity and with accompanying increase of air velocity index; bronchospirometry gave no indication of the triad of severe restriction of oxygen uptake, relative hyperventilation, and moderate reduction of vital capacity usually associated with unilateral pleural disease. Some months after operation pulmonary function was normal in every respect (Table III), but, as is

true of all studies of this type, more time must elapse before the final results regarding both pulmonary function and recurrence of spontaneous pneumothorax can be fully evaluated.

SUMMARY AND CONCLUSIONS

1. The presently accepted treatment for spontaneous pneumothorax and its complications has been reviewed.

2. Exploratory thoracotomy and local wedge or segmental excision of the offending lesion appear to be the treatments of choice for recurrent spontaneous pneumothorax.

3. Parietal pleurectomy was devised as definitive treatment when exploration reveals subpleural involvement which is too extensive to make excision of blebs, cysts, or vesicles practical or advisable from the pulmonary function standpoint. The operation may also be applicable in patients with recurrent or chronic pneumothorax who prove to have no detectable abnormality of the lung surface or show multiple cracks or leaks of the visceral pleura without associated blebs.

4. Pleurectomy is preferred over chemically or mechanically induced pleuritis because it entails fewer complications and shortens hospitalization and because the potential pleural space and thus the chance of recurrence are eliminated.

5. Complications were minimal after 9 total or subtotal parietal pleurectomies. Objective studies of ventilatory function and bronchospirometry revealed no measurable loss of pulmonary function. Attempts at postoperative induction of artificial pneumothorax proved unsuccessful, and there have been no recurrences of spontaneous pneumothorax on the side operated upon.

REFERENCES

1. Brock, R. C. Recurrent and chronic spontaneous pneumothorax. Thorax, Lond., 1948, 3: 88.
2. Gaensler, E. A. Medical progress: clinical pulmonary physiology. N. England J. M., 1955, 252: 177, 221, 264.
3. Gaensler, E. A., and Strieder, J. W. Pulmonary function before and after extrapleural pneumothorax. J. Thorac. Surg., 1950, 20: 774.
4. Idem. Streptokinase-streptodornase in the treatment of extrapleural hematoma complicating extrapleural pneumothorax. Am. Rev. Tuberc., 1951, 63: 547.
5. Gaensler, E. A., Watson, T. R., Jr., and Patton, W. E. Bronchospirometry—VI, results of 1,089 examinations. J. Laborat. Clin. M., 1953, 41: 436.
6. Leach, J. E. Pneumothorax in young adult males: statistics on 126 cases. Arch. Int. M., 1945, 76: 264.
7. Maxwell, J. The production of pleural adhesions by kaolin injection. Thorax, Lond., 1954, 9: 10.
8. Myers, J. A. Simple spontaneous pneumothorax. Dis. Chest, 1954, 26: 420.
9. Paul, J. S., Beattie, E. J., Jr., and Blades, B. Lung function studies in poudrage treatment of recurrent spontaneous pneumothorax. J. Thorac. Surg., 1951, 22: 52.
10. Perry, K. M. A. On spontaneous pneumothorax. Q. J. Med., Oxf., 1939, 8: 1.
11. Schneider, L., and Reissman, I. I. Idiopathic spontaneous pneumothorax: history of 100 unselected cases. Radiology, 1945, 44: 485.
12. Spengler, L. Zur Chirurgie des Pneumothorax. Beitr. klin. Chir., 1906, 49: 80.
13. Waterman, D. H. Commenting on Crenshaw, G. L. Etiology, treatment and surgical indications of nontuberculous, nontraumatic spontaneous pneumothorax. Dis. Chest, 1950, 17: 369.
14. Watson, T. R., Jr., and Gaensler, E. A. Immediate and late respiratory impairment due to selective staged thoracoplasty, extraperiosteal plombage and extrapleural conversion thoracoplasty. Tr. Nat. Tuberc. Ass., N. Y., 1952, 48: 267.

THE FATE OF AUTOGENOUS SKIN TUBES AS AORTA GRAFTS

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ALTHOUGH CARREL, as early as 1907, used peritoneum to repair an aortic defect in a cat, not until the last few years has there been an impetus to the use of various types of autogenous tissues, experimentally and clinically, to bridge vascular defects. Recently, vessels have been fashioned from autologous pericardium, connective tissue, rectus sheath, veins, and compilations of segments of small arteries. The hope has been that tissue readily available, without the disadvantage in procurement, sterility, preservation, and reactivity of homologous vessels, could be found. In the search for such a material in our laboratory, it was thought that autogenous skin tubes deserved consideration. Since perhaps the superiority of homologous blood vessels over synthetic materials is due to the presence of elastic tissue in the former, it was believed that skin which contains elastic fibers might be superior to other autologous tissue.

Subsequent to the onset of this study, Hardin reported his experiences with the use of tubed dermal grafts in 11 animals (4 thoracic, 4 abdominal, 3 ileofemoral). Also, Horton and his colleagues demonstrated the fate of dermal skin grafts placed on the surface of the thoracic aorta to add strength and thickness to the vessel wall. In this report reference was made to unpublished results using tubed dermal grafts to repair arterial defects.

The purpose of this paper is to present our experiences with the use of dermal tubes to replace segments of the abdominal aorta in 25 dogs, survivors being followed for at least 6 months after the operative procedure was carried out.

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METHOD

Mongrel dogs of both sexes, averaging 21 kilograms in weight, were used in this study. All were operated upon under pentobarbital sodium anesthesia. The anterior abdominal wall was closely shaven and was prepared with soap and water, tincture of iodine, and 70 per cent alcohol. Using a sterile metal rule and a scalpel handle as a marker, a rectangle 3.5 centimeters wide and 6 to 10 centimeters long was delineated so that the medial side was about 1 centimeter to the right of the midline of the abdomen. Dermatome cement was applied to the area of skin within the confines of the rectangle, and to the central area of the Padgett-Hood dermatome drum. After 5 minutes of contact of drum with skin, a split thickness flap 10/1000 of an inch in thickness was cut. This flap was removed from the drum, leaving the superior short side of the rectangle in contact with the contiguous skin. The underlying dermal rectangle was removed with a sharp scalpel. The split thickness flap was sutured back to cover the defect of the donor site, and the subcutaneous tissue adherent to the under surface of the dermal graft was removed by sharp dissection. A piece of glass tubing, 1 centimeter in diameter, was used as a stent. The piece of dermis was placed around the glass and the two long sides were sewed together with a continuous everting stitch of No. 5-0 silk. In the first 5 skin tubes so prepared, the superficial corium was turned in to form the luminal surface of the graft. In the next 20, the deep surface of the skin, free of fat and connective tissue, formed

FIG. 1. Aneurysmal dilatation in animal 6 months after insertion of skin tube.

the inner surface of the tube. All grafts were placed in normal saline while the aorta was prepared for segmental resection and grafting. The aorta was freed of the surrounding tissue and a straight piece, 2.5 to 3 centimeters, was resected midway between the renal arteries and bifurcation. The skin graft was inserted by the use of continuous over-and-over No. 5-0 silk sutures. Care was taken so that the graft was inserted neither under tension nor so that it was too lax when the clamps were removed and it became distended with blood. The slight amount of bleeding that occurred at the suture lines following removal of the clamps was readily controlled with the light pressure of a gauze sponge. All grafts and aortas distally were seen to pulsate. Posterior peritoneum was sutured over the grafted aorta and the abdomen was closed in layers.

Postoperatively, aortograms were performed at intervals and femoral pulses were palpated frequently. At death or sacrifice of the animals, sections for histologic examination were taken.

Portions of the host vessel and skin grafts were fixed in 10 per cent neutral formalin dehydrated, and infiltrated with paraffin in the usual manner. Sections were stained with hematoxylin and eosin, Verhoeff-van Gieson elastic tissue method, and Masson trichrome technique. On occasion, Perls' reaction for iron was performed on paraffin sections. Frozen sections were prepared from wet formalin fixed tissue and stained with oil red O for the demonstration of lipid.

RESULTS

The fate of 25 animals with replacement of aortic segments by autogenous skin is summarized as follows: Nine dogs survived 6 to 8 months; 7 with grafts remaining patent, 2 in which thrombosis developed. Death due to postoperative hemorrhage occurred in 15 animals; in 11 within 2 to 16 days, in 4 within 16 to 55 days. One animal died on the thirty-sixth day following an aortogram.

Of the 5 dogs having segments of aorta replaced by skin tubes so constructed that the superficial corium became the luminal surface, only 1 survived for more than 10 days. Four died from massive hemorrhage on the third, fourth, fourth, and ninth postoperative days. In addition to thrombosis, extensive necrosis of the skin occurred in each, so that the tube was almost completely disintegrated. An aortogram performed 2 months postoperatively on the 1 surviving animal demonstrated complete occlusion of the graft, and at sacrifice there was a firm thrombus present.

Results were better in the 20 animals in which the deep dermal surface formed the lumen. Seven survived for from 6 to 8 months with grafts remaining patent as proved by aortogram and sacrifice of the animal. One dog, as shown by the aortogram at the end of 4½ months, had a nonpatent graft; another, whose graft was pat-

FIG. 2. Aortograms: a, 30 days after insertion of skin graft; b, 4 months after insertion of skin graft; c and d, 6 months after insertion of skin graft.

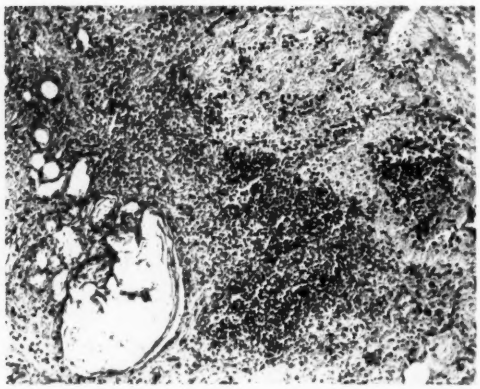

FIG. 3. Luminal surface of skin graft revealing masses of keratin and hair shafts which were observed within thrombus. ×73.

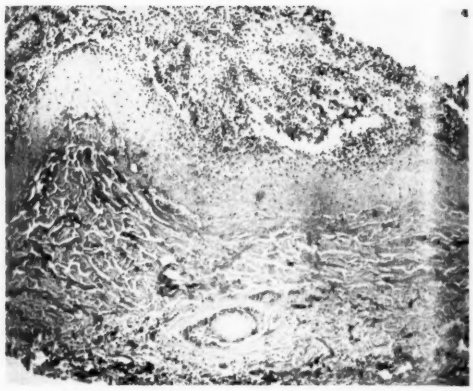

FIG. 5. Section of skin graft after 3 weeks revealing dense fibrin masses on the luminal surface and degenerating hair follicle in corium. ×38.

ent, died following an aortogram performed 36 days after operation. Aneurysmal dilatation of the grafts was a prominent feature after several weeks (Fig. 1). Graft walls were moderately pliable, but the adventitial surfaces were thickened by fibrous connective tissue which extended for varying distances along the host vessel.

The remaining 11 animals died of hemorrhage between the second and fifty-fifth day after operation, the average survival time being 16 days. In these animals, necrosis of the skin tube was a frequent finding, but thrombosis was less extensive than in the first group. After the first few weeks, rupture of an aneurysmal sac was the most common cause of hemorrhage in this group. In only 1 of the entire group was there a question as to the hemorrhage being due to disruption of the suture line at the graft aortic anastomosis. Aortograms performed at periodic intervals in the surviving animals have demonstrated progressive distortion of the patent grafts (Fig. 2).

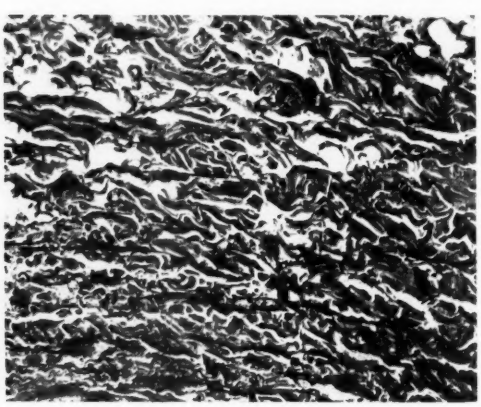

FIG. 4. Corium of graft after transplantation for 1 week demonstrating elastic fibers. Verhoeff-van Gieson stain, ×88.

Histologic examination of the grafts revealed extensive alteration of the original architecture. Epidermis was found in only 1 example in which the outer corium was utilized as the luminal surface, and in this instance it was focal and apparently degenerating after 1 week of transplantation. Thrombosis was apparent in all examples of this type of graft at this period, and in several instances resulted in complete occlusion. Masses of keratin and hair shafts were occasionally observed within the thrombi (Fig. 3). On the other hand, thrombosis, although present, did not appear as extensive in those grafts in which the deep corium was utilized as a luminal surface. The corium of both types of grafts was heavily infiltrated with neutrophils, lymphocytes, and moderate numbers of plasma cells, particularly at the luminal surface, 1 week following transplan-

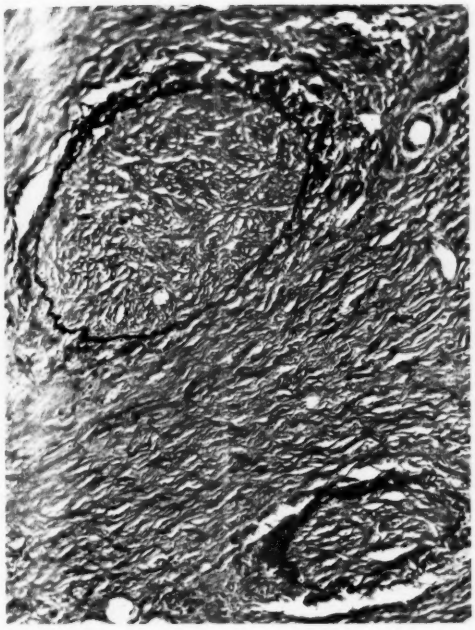

FIG. 6. Organized thrombi within vessels of deep corium 3 weeks following transplantation. The elastic lamina is distinct. Verhoeff-van Gieson stain, ×90.

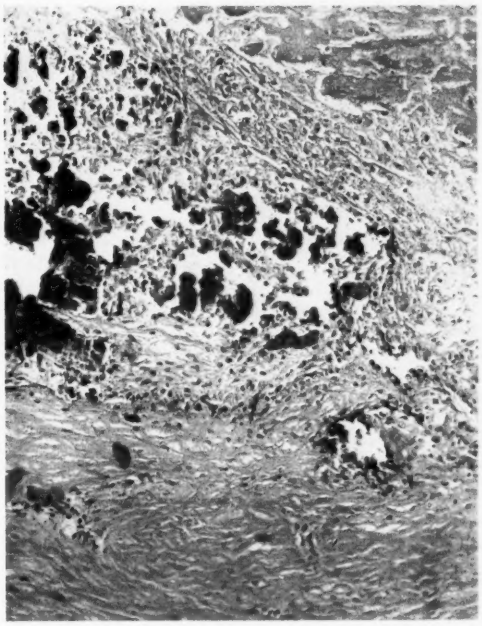

FIG. 7. Section through skin graft 6 months after transplantation revealing thrombus at top right and focus of calcification in corium. ×90.

tation. This exudate was of less intensity in deeper layers, being particularly located about and within hair follicles. These latter revealed necrosis of the root cells and in some areas only hair shafts were noted embedded in the dense collagen of the corium. Focal degeneration of the collagen of the corium was noted in both types of graft after 1 week. Elastic fibers appeared discontinuous and sparse (Fig. 4). The deep vessels did not reveal pathologic change at this particular time.

There was little difference in the histologic appearance of the grafts after 2 and 3 weeks of transplantation from that already noted. Beginning organization of the luminal thrombi was apparent, and fibrin masses, which were previously loosely arranged, were more dense (Fig. 5). Cellular elements of the hair roots were, for the most part, absent although hair shafts persisted in the corium. This latter, in some examples, was necrotic in areas, being heavily infiltrated with inflammatory exudate and hemorrhage. Elastic fibers were still demonstrable in less severely involved zones. The deeper portions of the corium were thickened by relatively acellular connective tissue and contained a moderate exudate. Many of the vessels within this zone contained thrombi, some of which appeared organized (Fig. 6), and medial hypertrophy was conspicuous. The intimal layer of the host vessel was covered for a short distance by a connective tissue pannus apparently arising from the reparative zones at the lines of anastomosis. The media of the host vessel appeared well preserved.

After 2 months the skin grafts were comprised of dense acellular collagen containing scattered, discontinuous elastic tissue fibers. Only a few hair shafts remained, and the exudate noted previously was diminished. The luminal thrombi and vascular changes noted previously were also evident at this time.

In addition to these, the skin grafts after 6 months contained collections of macrophages within the luminal thrombi. Many of these contained lipid or hemosiderin or melanin pigment within their cytoplasms, the latter apparently derived from degenerating hair shafts. Focal calcification of the corium was noted in 2 instances (Fig. 7). Elastic fibers appeared similar to those noted previously. A dense, relatively acellular connective tissue extended from the graft along the adventitial surface of the host vessels.

COMMENT AND CONCLUSION

From these findings it may be concluded that the use of autogenous tubed dermal grafts to replace segments of aorta is highly unsatisfactory. In animals in which grafts were fashioned so that the external corium formed the luminal surface, results were 100 per cent poor. When the deep dermal surface formed the lumen, 35 per cent of the grafts inserted were patent after 6 months, but in these there was such distortion, aneurysmal dilatation, and histologic change to the tubes that one would necessarily consider the results to be far from satisfactory. It is conceivable that such grafts might be resorted to in humans only as a last resort in an emergency in which no other replacement material is available. If these findings are representative of what might occur in the human, they could be expected to function at best for only a short time. Apparently the elastic fibers of the skin are inadequate to maintain luminal constancy. Should thrombosis and early necrosis not occur, aneurysmal dilatation even to the point of rupture might well be expected to take place.

It is difficult to explain why some of the grafts survived initially while others sloughed. Thrombosis of the vessels within the subcutaneous tissue must play a role, for microscopic examination revealed this not to be as extensive in the longer survivors.

SUMMARY

Segments of abdominal aorta from 25 dogs were replaced by tubed grafts fashioned of autogenous dermis taken from the anterior abdominal wall. When the graft was prepared so that the outer corium formed the luminal surface, results were universally poor, with thrombosis and sloughing of the graft occurring. When the deep corium was the "interval" surface, 35 per cent of the grafts remained patent for over 6 months. Aneurysmal dilatation, distortion, and histologic changes were so great as to make it seem undesirable to use such tissue to replace defects in the human aorta.

REFERENCES

1. Carrel, A. Surgery of blood vessels. Bull. Johns Hopkins Hosp., 1907, 18: 181.
2. Hardin, C. A. Dermal grafts in the experimental repair of vascular defects. Angiology, 1955, 6: 47.
3. Horton, C. E., Campbell, Frank, Connor, Richard, McWhirt, Joseph, and Pickerell, Kenneth. Behavior of split thickness, dermal, and full thickness skin grafts in thoracic cavity. Arch. Surg., 1955, 70: 221.

SIALOGRAPHY

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SIALOGRAPHY is the delineation of the salivary duct system by the injection of a radiopaque medium. Although limited in scope, the method has definite indications in patients with obscure swelling or pain in the region of the salivary glands.

The history of diagnostic sialography began in 1904 when Charpy first demonstrated the parotid duct system on an isolated gland. In 1913, Arcelin injected bismuth into a submaxillary duct to demonstrate a calculus (3). In 1925, Carlsten, Uslenghi, and Barsony used this procedure apparently independently of each other. In 1926, Jacobovici, Popolitza, and Albu and Wiskovsky reported cases of patients upon whom sialography was performed. Keith in 1928 reported the first case which was done in the United States. By 1932 Rocchi and Barsky and Silberman had reported 9 and 8 cases respectively. Blady and Hocker in 1938 collected sialograms on 99 patients, and they attempted to establish definite criteria for diagnosis by the correlation of the roentgenologic appearance and the surgical pathology. In this series there were 23 sialograms showing normal parotid glands and 76, neoplasms. One year later, they added 38 nonneoplastic cases to the literature (4). The largest single series to date, 110 cases, was reported by Schulz and Weisberger from the Massachusetts General Hospital.

Swinburne raised a pertinent question concerning terminology. He contended, and with some justification, that the procedure should be called sialoangiography rather than sialography and that the condition of saccular dilatation of the ducts be termed sialoangiectasis rather than sialectasis. The term sialodochography also has been suggested. Without disputing the merits of the contention of Swinburne and others, we have continued the usage of sialography and sialectasis because of their simplicity and wide acceptance.

Since the majority of salivary tissue tumors occur in the parotid gland, (70 per cent in the Hendrick, Ward, and Lacy series), attention is focused in this study on the parotid gland only. From the files of the Johns Hopkins Hospital and the private practice of one of us (G. E. W.), we have collected 53 cases of patients upon whom sialography had been performed. Patients without definite diagnosis and adequate follow-up examination have been excluded. In 38 patients, surgery had been performed and the basis for final classification was gross and microscopic pathology. In 15 patients, conservative measures were elected and sufficient time was allowed for observation so that the clinical course could be considered a verification of the diagnosis. Although in a certain number of these patients the sialographic findings appeared normal subsequent surgery revealed the presence of disease. Roentgenologic examination did not reveal these abnormalities because the lesions were located outside the gland proper and were of small size. An analysis of this series by diagnosis is presented in Table I.

TECHNIQUE

Injection. No specific premedication is required. It is not necessary to prohibit eating before examination. A prepared kit should include the following: 2 cannulas (lacrimal duct type) with an orifice of at least 0.5 millimeter internal diameter, a long-barrelled

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FIG. 1. A metal cast of the right parotid gland is shown in its anatomic position. Note how the anterior portion of the gland is flat and parallel to the ramus of the mandible while the posterior ducts sweep around medially and lie behind and somewhat deep to the ramus.

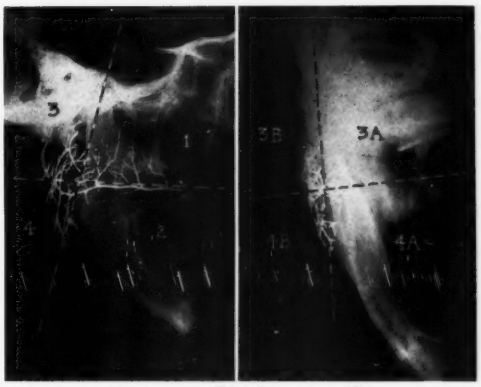
5 cubic centimeter syringe, preferably Luer-Lok, a set of lacrimal duct dilators, sizes 1 to 4, sponges 4 by 4 inches, head mirror and light, and contrast substance, such as iodized oil (iodochlorol) or the newer resorbable media (oily dionosil). The orifice of the parotid duct is on the inner surface of the buccal mucosa at the level of the second upper molar tooth. The buccal papilla usually contains, and sometimes overhangs, the orifice. A local anesthetic may be used but is not necessary. If there is difficulty in identifying the orifice of the duct, the gland should be massaged in order to observe the ejection of saliva. The stoma can be probed with the graduated series of lacrimal dilators until No. 3 or No. 4 is reached. When sufficiently dilated, the cannula is placed in the duct, the loaded syringe is attached, and approximately 1.75 cubic centimeters are injected slowly and steadily. Most patients complain of a disagreeable sensation in the gland before this entire amount is given. By pausing from time to time before the injection is completed, the patient will be spared all but minimal discomfort.

TABLE I.—DISTRIBUTION OF CASES BY DIAGNOSIS

	No. of cases
Normal	8
Inflammations	
Subacute parotitis	5
Chronic parotitis	11
Abscess	2
Tumors	
Benign mixed	8
Malignant mixed	2
Papillary cystadenoma lymphomatosum (Warthin's tumor)	3
Carcinomas	5
Lymphomas	1
Lipomas	1
Miscellaneous pathology	
Fatty infiltration	1
Von Mikulicz's disease	1
Organizing hemorrhage	2
Cyst of pterygoid fossa	1
Retention cyst	2
Total	53

Roentgen. The patient is immediately positioned for the following roentgenograms: a true anteroposterior view, a true lateral view, basal view of the skull, and a tangential view to be varied according to the area involved.

Localization of lesions. The anterior portion of the parotid gland is flat and overlies the ramus of the mandible. The remainder of the gland extends posteriorly and medially between the mandible and the mastoid process. This portion is frequently called the retromandibular "lobe" (Fig. 1). During the course of this study the necessity for exact localization of lesions was evident. We have devised a system based upon three planes of reference rather than on standard anatomic points. The first, a transverse plane, passes horizontally through Stensen's duct to bisect the gland into a superior and inferior portion. The second plane is coronal and corresponds to the posterior margin of the mandibular ramus. This plane divides the gland into an anterior flat portion and a posterior thick portion. The third plane is sagittal at the lateral surface of the mandibular ramus and divides the posterior part of the gland into the lateral or superficial portion and the medial or deep portion.



a FIG. 2 b

FIG. 2. a, Lateral view. The gland in this cadaveric specimen has been injected with a low melting point metal. The vertical line coincides with the posterior border of the ascending ramus of the mandible and divides the gland into an anterior and posterior portion. The horizontal line passing along the main duct divides the gland into a superior and inferior portion. (*1*) anterior superior portion; (*2*) anterior inferior portion; (*3*) posterior superior portion; (*4*) posterior inferior portion. b, Anteroposterior view. The vertical line coincides with the lateral margin of the ramus of the mandible and separates the posterior portion of the gland into a deep and superficial portion. The horizontal line which passes through the main duct separates the posterior portion of the gland into a superior and inferior portion. (*3A*) posterior deep superior portion; (*3B*) posterior superficial superior portion; (*4A*) posterior deep inferior portion; (*4B*) posterior superficial inferior portion.

On the lateral projection, the four glandular quadrants formed by the transverse and coronal planes can be seen, i.e., (*1*) anterior superior, (*2*) anterior inferior, (*3*) posterior superior, and (*4*) posterior inferior (Fig. 2). On the anteroposterior view, the sagittal plane subdivides the posterior part of the gland into: (*3A*) deep superior, (*3B*) superficial superior, (*4A*) deep inferior, and (*4B*) superficial inferior (Fig. 2b). Thus, the parotid gland is composed of 6 portions as follows: anterior superior, anterior inferior, posterior superficial superior, posterior deep superior, posterior superficial inferior, and posterior deep inferior.

THE NORMAL SIALOGRAM AND PITFALLS IN INTERPRETATION

The size and shape of the normal parotid gland exhibits marked variations which are also reflected in the size, shape, and branching of the duct system. The normal Stensen's duct does not exceed 3 millimeters in diameter and usually points toward the first or second cervical vertebra. When the duct system is incompletely filled with opaque medium the stark "winter tree" type of arborization is seen because of the lack of filling of the terminal branches. When too much opaque medium is used there is a diffuse "summer tree" appearance which suggests that the terminal ductules and perhaps the acini are filled. When the injection pressure is too great, particularly with water soluble opaque media such as diodrast or dionosil, irregular interstitial collections may be seen which are presumably caused by a rupture of the finer ducts with spillage of the opaque medium into the parenchyma of the gland. These collections are generally irregular in outline and have hazy, indistinct borders which appear to follow tissue planes.

FIG. 3.

FIG. 3. Anteroposterior view. Features: (*a*) the most lateral portion of the gland is 28 millimeters from the ramus of the mandible; (*b*) the posterior inferior ducts show a tendency to stretching and straightening; (*c*) the posterior part of the main duct is displaced laterally and superiorly. Diagnosis: benign mixed tumor. Note: this tumor arose in the posterior deep inferior portion of the gland.

FIG. 4.

FIG. 4. Lateral view. Features: (*a*) slight local angulation of the main duct; (*b*) radiolucent area in the anterior superior portion of the gland; (*c*) the ducts are stretched and wrapped around the mass; (*d*) extravasations at the periphery of the mass; (*e*) the ducts with essentially normal pattern. Diagnosis: benign mixed tumor. Note: this tumor arose in the anterior superior portion of the gland.

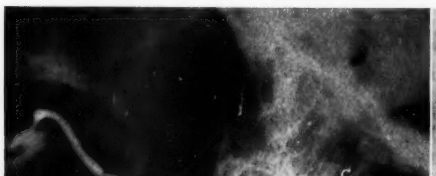


FIG. 5.

FIG. 6.

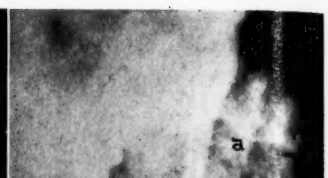


FIG. 7.

FIG. 5. Lateral view. Features: (*a*) the main duct is markedly tortuous; (*b*) radiolucent area in the posterior inferior portion of the gland; (*c*) the ducts stretched around the mass. Diagnosis: benign mixed tumor. Note: this tumor arose in the posterior inferior portion of the gland.

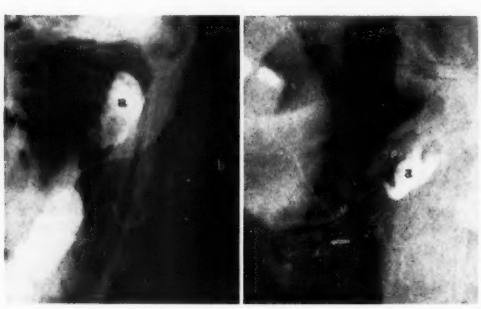
FIG. 6. Anteroposterior view. Features: (*a*) the ducts stretched and straightened; (*b*) extravasations around the periphery of an area containing no ducts. Diagnosis: benign mixed tumor. Note: this tumor arose in the posterior superficial superior portion of the gland.

FIG. 7. Anteroposterior view. Features: (*a*) the "summer tree" appearance of an overfilled gland; (*b*) radiolucent area. Diagnosis: benign mixed tumor. Note: that this tumor arose in the anterior inferior portion of the gland.

The arch of the atlas in the direct lateral view will frequently be superimposed on the parotid tree. Because of the sclerotic cortical bone and the radiolucent marrow it may be misinterpreted as a cavity. Scout films, essential in every sialographic study, will clarify this point. Intraoral spillage and residual opaque medium in the valleculae or piriform sinuses occasionally will give bizarre shadows.

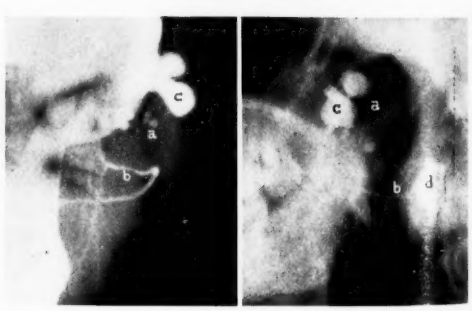
CRITERIA FOR DIAGNOSIS

Sialographic lesions may be divided into three types: (1) space-taking lesions extrinsic



a b

FIG. 8. a, Anteroposterior view. b, Oblique view. Features: (*a*) radio-opaque area in the posterior deep superior portion of the gland—smooth and distinct in outline, uniform in density; (*b*) the most lateral portion of the gland is 22 millimeters from the ramus of the mandible. Diagnosis: papillary cystadenoma lymphomatosum (Warthin's tumor). Note: the absence of other inflammatory changes and the form and outline of the cavity tend to rule out the diagnoses of abscess and extravasation respectively.



a b

FIG. 9. a, Anteroposterior view. b, Lateral view. Features: (*a*) radiolucent area with no traversing ducts; (*b*) the posterior part of the main duct appears to bend around this area; (*c*) radio-opaque areas in the center of the radiolucent mass—multilocular, smooth in outline, uniform in density; (*d*) the arch of the atlas. Diagnosis: abscess. Note: the presence of multilocular and discrete groups of cavities within an obvious mass is indicative of abscess formation. Inflammatory sacculations are not marked in this film.

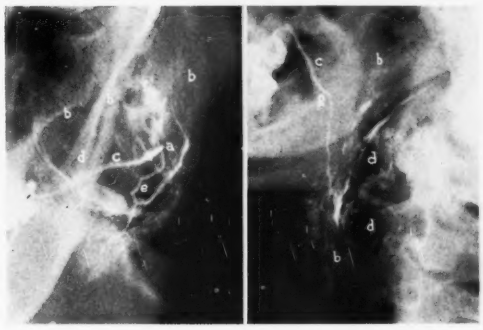
to the parotid gland and exerting pressure through the gland capsule, (2) space-taking lesions intrinsic to the parotid gland and exerting pressure on the duct system, and (3) abnormalities within the duct system itself.

1. *Extrinsic lesions.* Extrinsic lesions which may cause abnormal sialograms are: metastatic lymph nodes adjacent to the gland, cysts or tumors in the pterygoid fossa, hemorrhage in adjacent muscles, tumors of the mandible, and lipomas in the buccal or cervical fat. In these cases the entire gland or a large portion of it appears to be displaced en masse. The lesion itself usually blends with the soft tissues and unless it is composed of bone or fat or contains calcium deposits, it cannot be differentiated from the surrounding bed. While the gross configuration of the gland may be abnormal, rarely is there any appreciable distortion of the duct pattern.

When on a true anteroposterior view any part of the main duct is more than 15 millimeters from the lateral margin of the ramus of the mandible, a mass medial to the duct or anterior portions of the gland is to be suspected. Also a distance of 20 millimeters from the most lateral portion of the intraglandular duct pattern to the ramus is presumptive evidence of a mass situated deep to the posterior portion of the gland (Figs. 3, 8, 10).

2. *Intrinsic lesions.* Mixed tumors, retention cysts, branchial cleft cysts, Warthin's tumors, abscesses, and all other benign and malignant tumors primary in the parotid gland are examples of intrinsic lesions. In these cases, the ducts are displaced at some focal point within the gland. The filled ducts appear to sweep around the mass and embrace it. Sometimes the ducts appear to be attenuated and stretched taut (Figs. 3, 4, 5, 6, 10a, and 10b).

When the gland has a summer tree appearance, an intrinsic lesion often takes the form of a radiolucent globular area (Fig. 7). Lesions such as abscesses or Warthin's tumors may excavate into the duct system. When this occurs large cavities may fill with contrast substance (Figs. 8a, 8b, 9a, and 9b). In-



a b

FIG. 10. a, Anteroposterior view. b, Lateral view. Features: (*a*) main duct is 17 millimeters from the mandible; (*b*) ducts that are stretched and straightened; (*c*) irregularity of the main duct; (*d*) a large radiolucent area containing no ducts; (*e*) "tenting" of the ducts at the periphery of this area; (*f*) calcification within this area (seen on scout films); (*g*) marked angulation of the main duct. Diagnosis: carcinoma. Note: this was a massive lesion, involving the entire gland.

frequently the benign or malignant nature of the mass can be diagnosed by roentgenologic appearance alone. Occasionally, malignancy may be suspect in a mass when the ducts are cut off sharply, tented, infiltrated, or irregularly distorted and stiffened (Fig. 10a).

3. *Abnormalities of the duct system.* Lesions belonging to this category are usually due to inflammatory processes. The mechanism that initiates the process may be infection, both retrograde and blood-borne, calculi, mumps, and ductal strictures. Dilatation and stric-

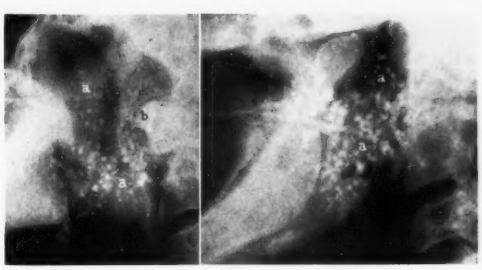


FIG. 11. FIG. 12.

FIG. 11. Lateral view. Features: (*a*) multiple minute sacculations; (*b*) arch of the atlas. Diagnosis: subacute parotitis. Note: the small size of the saccules indicate only minimal destruction of tissue.

FIG. 12. Lateral view. Features: (*a*) multiple small sacculations. Diagnosis: chronic parotitis.

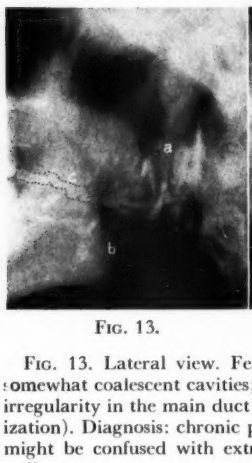


FIG. 13.

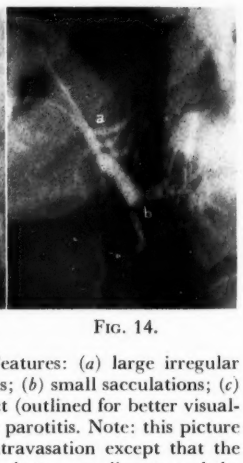


FIG. 14.

FIG. 13. Lateral view. Features: (*a*) large irregular somewhat coalescent cavities; (*b*) small sacculations; (*c*) irregularity in the main duct (outlined for better visualization). Diagnosis: chronic parotitis. Note: this picture might be confused with extravasation except that the radiopaque areas are somewhat more discrete and the outlines more distinct.

FIG. 14. Lateral view. Features: (*a*) minute sacculations along the course of the ducts; (*b*) marked variations in the diameters of the ducts. Diagnosis: chronic parotitis.

tures of Stensen's duct are readily apparent by sialography. Sialectasis, which apparently is a result of any inflammation of the gland, also produces a distinct roentgenologic pattern-puddling of the opaque medium in the dilated terminal branches of the ducts.

TABLE II.—DIFFERENTIAL DIAGNOSIS BETWEEN NEOPLASMS AND INFLAMMATORY DISEASES

History	*Benign tumors*	*Malignant tumors*	*Inflammations*
Clinical history			
Rate of growth	Slow-years	Rapid-months	Rapid-days to weeks
Age, years	Between 20 and 45	Average, 55	All ages
Sex	No essential difference	More frequent in females	No essential difference
Pain	Usually absent	Very commonly present early	Usually present early
Physical examination			
Fixation	Freely movable in the superficially located; more limited movement in the deeper ones	Often fixed to skin, deep structures, and bone	Rarely fixed to any structures
Facial nerve paralysis	Unusual	Present in 40 per cent of the cases	Rare
Consistency	Firm, cystic, nodular	Stony hard, or in small lesions may resemble benign tumors	Usually smooth, diffusely enlarged

Modified from *Tumors of the Head and Neck*, by Ward and Hendrick. Baltimore: Williams & Wilkins, 1950.

Sacculations vary considerably in size according to the degree of virulence and chronicity of the infection. The size of the saccules may range from 2 to several millimeters in diameter. Occasionally, they may coalesce to form multiloculated cavities at which point they may be considered abscesses (Figs. 11, 12, and 13). Often in inflammatory diseases the larger ducts will show an irregularity in outline and diameter. These changes probably have the same pathogenesis as sacculations in the gland periphery (Fig. 14).

SURGICAL IMPLICATIONS OF SIALOGRAPHY

While sialography can be of inestimable value in the diagnosis of disease of the salivary glands, it should not be abused as a short-cut method of diagnosis. Even with a meticulous history, physical examination, and laboratory tests, the pitfalls in diagnosis are great. The interpretation of sialograms without adequate clinical information amounts to a sterile exercise, while failure to realize the potentialities of the method may be rendering an injustice to the patient. Not infrequently sialography will avoid an operation or aid in the planning of the most appropriate type of surgery.

In order to summarize the important clinical features which may aid in the differential diagnosis, Tabe II was evolved.

It will be noted that acute inflammations are characterized by diffuse swelling, heat, pain, rapid variation in size, and some tendency to bilateral involvement. Chronic inflammations present a swelling, unilateral or bilateral, with or without pain, diffuse or localized, and which may vary in size with salivation. A benign tumor appears as a slowly growing, discrete firm mass without pain. Patients with malignant tumors usually have a story of rapid, unilateral, painful, and hard swelling. Malignant tumors are more frequent in females; fixation to surrounding structures is common, and facial nerve palsy is present in 40 per cent of the patients. Mixed tumors with malignant changes may resemble benign tumors when small, or malignant tumors when large and invasive

SUMMARY

The results of a careful study of 53 sialograms of the parotid gland have been presented. Sialography has been found to be of definite diagnostic value in cases of suspected parotid disease. Sialography can indicate an inflammatory process and is capable of revealing a neoplasm in its exact location. In certain cases of carcinoma, sialography may even suggest the malignant nature of the tumor. Sialography may be an aid in differentiating lesions of nearby structures from those involving the gland itself.

REFERENCES

1. Barsky, A. J., and Silberman, H. Roentgen visualization of parotid gland by means of lipiodol injection. Ann. Surg., 1932, 95: 46.
2. Barsony, T. Idiopathic dilatation of Stenson's duct. Klin. Wschr., 1925, 4: 2500.
3. Blady, J. V., and Hocker, A. F. Sialography, its technique and application in roentgen study of neoplasms of parotid gland. Surg. Gyn. Obst., 1938, 67: 777.
4. Idem. Application of sialography in non-neoplastic diseases of parotid gland. Radiology, 1939, 32: 131.
5. Carlsten, D. B. Lipiodol injection in duct of salivary glands. Acta radiol., Stockh., 1926, 6: 221.
6. Hendrick, J. W., Ward, G. E., and Lacy, M. Salivary tissue neoplasms. Am. J. Surg., 1951, 81: 373–386.
7. Jacobovici, Popolitza, and Albu. Sialography. Presse méd., 1926, 34: 1188.
8. Keith, H. M. Injection of parotid gland with iodized oil. J. Am. M. Ass., 1928, 90: 1270.
9. Rocchi, F. Scialografia normale e patologica. Riv. radiol., 1930, 2: 1.
10. Schulz, M. D., and Weisberger, D. Sialogram in diagnosis of swelling about salivary glands. Surg. Clin. N. America, 1947, 27: 1156.
11. Swinburne, G. Sialoangiectasis. Brit. J. Surg., 1940, 27: 713.
12. Uslenghi, J. P. Nueva tecnica para la investigación radiólogica de las glándulas salivales. Sem. méd., B. Air., 1925, 32: 41.
13. Wiskovsky, B. Sialodochografie. Zbl. Hals & c. Heilk., 1926, 8: 320.

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TREATMENT OF CANCER OF THE NASAL CAVITY AND PARANASAL SINUSES

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MALIGNANT TUMORS of the paranasal sinuses and nasal fossa have their origin, in most instances, in the lining membrane of these cavities and their symptoms are comparable.

This group of cancers is of clinical importance to the practitioner, dentist, and otolaryngologist as well as to other medical specialists. When a diagnosis is established early and efficient therapy is administered, including reconstructive surgery and prosthetic appliances, conditions such as poor phonation, difficulty in swallowing, mastication, and cosmetic disfigurement are eliminated.

Treatment should be planned to destroy the cancer and institute such measures as are necessary to rehabilitate the patient. Justification for enlarging the scope of treatment to include resection of the superior maxilla and in many patients exenteration of the orbit and adjacent structures is based on fundamental anatomic, clinical, pathologic, and biologic surgical principles.

Radiation therapy does not destroy primary cancer in the paranasal sinuses in a sufficient number of cases to warrant its use alone. This is also true of radical surgical excision of the superior maxilla, with or without exenteration of the orbit. The utilization of a combination of the modalities of therapy should give a more substantial nonrecurrence rate and removes the complications resulting from extensive radiation when used alone.

INCIDENCE AND ETIOLOGIC FACTORS

It is estimated that malignant tumors of the nasal fossa and paranasal sinuses account for 1 per cent of human cancer.

Cancer of the paranasal sinuses and nasal fossa are frequently encountered in the Mexican population which is comparable to the high incidence of malignant tumors of the nasopharynx observed in the oriental races.

All ages may be affected with the greatest incidence occurring in individuals between 50 and 70 years old. Men are more frequently involved than women in a ratio of 2 to 1. One case in a child, a 6 year old female with fibromyxosarcoma (Fig. 1), another, in a 12 year old female with lymphosarcoma, both of the nasal cavity, have been encountered. Ward and Hendrick,[1] presenting tumors of the paranasal sinuses from the Johns Hopkins Hospital, reported a male 15 years of age with basal cell carcinoma of the superior maxilla.

In this series of 72 cases, no definite etiologic factors were discovered. Sixty patients had histories of nasal infection, polyps, allergic rhinitis, and sinusitis which had been present for long periods of time. Chronic sinusitis and nasal polyps are frequently encountered but there is no apparent relationship between these conditions and cancer; smoking is not considered as an etiologic factor.

ANATOMY AND LYMPHATICS

A detailed knowledge of the anatomy of the nasal fossa and paranasal sinuses contributes greatly to the interpretation of early symptoms of cancer involving these structures. Clinically and physiologically, the nasal cavity is divided into a superior or olfactory and an inferior or respiratory area. The nasal mucous membrane is continuous with that of the paranasal sinuses, lacrimal duct, and nasopharynx; it contains a dis-

[1]WARD, G. E., and HENDRICK, J. W. Tumors of the Head and Neck. Baltimore: Williams & Wilkins Co., 1950.

tinct basement membrane with lymphoid tissue and mucous, goblet, and pigment cells. The latter serve as the origin of malignant melanoma when this type of tumor is encountered in this location.

The maxillary antrum is a triangular, pyramidal shaped cavity occupying the center of the maxilla. Its base corresponds to the lateral wall of the nose and the apex extends to the malar bone. The walls of the antrum are thick in infancy and become thin in older individuals. The paranasal sinuses are lined with columnar ciliated epithelium containing many goblet and mucus forming cells and acinous glands which secrete a watery fluid.

The anterior lymphatics of the nasal fossa pass forward between the nasal cartilages to the teguments of the face where they become part of the superficial lymphatics of the skin of the nose and cheek. The posterior lymphatics of the nasal fossa, with those of the paranasal sinuses, gather into three trunks to terminate in the lymph nodes of the upper jugular chain. The upper jugular chain of lymph nodes are the earliest to become involved in carcinoma of the nasal fossa and paranasal sinuses.

PATHOLOGY

Most cancers of the nasal fossa and paranasal sinuses limit themselves to the area above the clavicles until late in the disease. They spread by direct extension and by the lymphatics and blood stream. The foremost method of extension is by direct invasion of adjacent structures. Extension to the lymph nodes occurs late in the disease in contrast to cancer involving the tongue and floor of the mouth.

The disease remains unilateral except in those cases involving the nasal septum and sphenoid and ethmoid cells. Only 2 patients of this group had metastases to the lymph nodes of the upper jugular chain from carcinoma of the antrum when first observed. Two other patients developed cervical metastases 2 and 3 years after the primary tumor was treated.

FIG. 1. Fibromyxosarcoma of the nasal fossa in a 6 year old female with nasal obstruction and discharge for 1 year. Tumor produced broadening of nose and grew out of anterior nares.

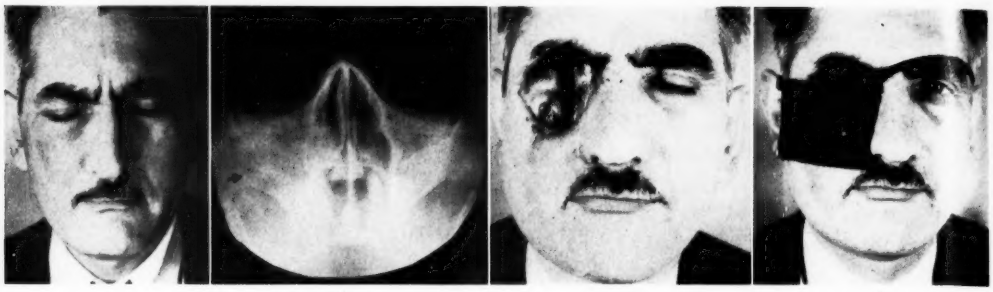
In this study of 72 cancers of the nasal fossa and paranasal sinuses, the following types were encountered: squamous cell carcinoma in 52 cases, adenocarcinoma in 4, cylindroma in 4, lymphoepithelioma in 4, round cell carcinoma in 2, fibromyxosarcoma in 2, lymphosarcoma in 2, malignant melanoma in 1, and fibrosarcoma in 1.

Eight cancers of this group involved the nasal fossa: 2 squamous cell carcinomas. 1 malignant melanoma, 2 lymphosarcomas, 1 lymphoepithelioma, 1 myxosarcoma, and 1 cylindroma.

In advanced carcinoma of the maxillary antrum the entire sinus becomes involved with invasion of the nasal cavity, orbit, cranium, alveolar process, and pterygomaxillary fossa with pansinusitis.

SYMPTOMS AND CLINICAL COURSE

Most patients with cancers of the nasal fossa and paranasal sinuses present themselves early for treatment following the onset of symptoms but, unfortunately, even after repeated examinations, the diagnosis may not be established until late in the



a b c d

FIG. 2. a, Squamous cell carcinoma involving suprastructure of right maxillary antrum causing fullness of right cheek and obliteration of nasolabial fold. Severe pain in maxilla was not relieved by extraction of teeth. b, Roentgenogram of maxillary sinuses demonstrating destruction of lateral antral wall and floor of orbit. c, Patient 1 year after resection of right superior maxilla and exenteration of orbital contents. d, Defect may be covered by prosthesis incorporated with spectacles or a simple black patch which is not objectionable.

course of the disease. In 46 of the 64 patients with carcinoma of the paranasal sinuses and in 5 with cancers of the nasal fossa, symptoms had been present for a period of at least 1 year before a definite diagnosis was established. The most common early symptoms of a benign or malignant tumor of the nasal fossa are nasal obstruction, discharge, and epistaxis. Later there is broadening of the bridge of the nose and ulceration of the skin, exophthalmos and, when both orbits are invaded, lateral displacement of the eyes. When the orifices of the sinuses are obstructed sinusitis results.

Cancer of the antrum usually originates in the floor in close association with the dental roots and nerves. When extension occurs there is invasion of the anterior sinus wall and soft tissues of the cheek producing obliteration of the nasolabial fold (Fig. 2), fullness of the cheek, widening of the upper gingiva, and loosening of the bicuspid and molar teeth. Perforation of the anterior wall of the antrum is demonstrated by palpation of the cheek; the soft tissues are swollen; the skin is edematous and, in advanced cases, it is infiltrated. When the floor of the antrum is destroyed, there is softening and swelling of the palate with ulceration into the mouth. When the tumor involves the posterior sinus wall, it invades the pterygomaxillary fossa.

When the roof of the sinus is involved, there is invasion of the floor of the orbit and malar bone. If the tumor occurs laterally, there is extension into the temporal fossa; if located medially, there is invasion into the naso-orbital region and sphenoid and ethmoid cells.

DIFFERENTIAL DIAGNOSIS

Several types of benign tumors and cysts involving the nasal fossa and paranasal sinuses must be differentiated from malignant tumors. These include polyps, adenomas, papillomas, nasopharyngeal fibromas, and rhinoscleromas. Other diseases to be considered are unilateral chronic sinusitis, odontogenic cysts, osteomas, ameloblastomas, and mucoceles. The symptoms of mucocele are intermittent attacks of unilateral sinusitis, pain in the region of the premolar and molar teeth, hyperesthesia and anesthesia of the teeth on the involved side, diplopia, and pressure necrosis of one or more antral walls.

TREATMENT

Treatment of cancer of the nasal fossa and paranasal sinuses depends on the age and general condition of the patient, location and extent of the tumor, and its histologic structure. A survey is made of the pathways of extension of the disease in order to determine if there is local or distant metastasis, or extension to the opposite side or to the cranium.

All patients are treated with radiation therapy or surgery or both. In advanced cases with extension of the primary cancer to the opposite side or to the cranial cavity or with distant metastasis, only palliative irradiation therapy is administered. It has been my practice to treat radiosensitive tumors, i.e., lymphosarcoma, transitional cell epithelioma, anaplastic epidermoid carcinoma of the nasal cavity, paranasal sinuses, or nasopharynx, with high voltage roentgen therapy.

Treatment of carcinoma of the nasal fossa. Squamous cell carcinoma of the mucocutaneous junction of the columella in most cases is treated by direct application of radium tubes placed against the growth with a small lead plate between the tubes and the ala of the nose to protect the latter. Malignant lesions posterior to the mucocutaneous juncture which are radiosensitive are treated with radiation therapy using 260 kilovolts, 30 milliamperes, 50 centimeters target skin distance, ½ to 1½ millimeter copper and 1 millimeter aluminum filters. Daily treatments are administered, the amount varying with the size of the field, to obtain a total of 4,000 to 5,000 roentgens. If necessary, 2 or 3 ports are utilized. The uninvolved, surrounding area is protected by a sheet of lead ¼ centimeter thick.

Radioresistant lesions on the nasal septum or turbinate bones are treated by electrosurgery and scalpel surgery using a lateral rhinotomy incision beginning in the floor of the nostril on the involved side and following around the ala of the nose in the nasolabial fold to the inner canthus of the eye (Fig. 3). The growth is carefully removed by electrosurgery allowing an adequate margin to insure complete removal. This method of therapy is particularly advisable for cancers on the posterior area of the septum or the posterior area of the turbinates; it gives good cosmetic results.

Extensive carcinomas that are radiosensitive are first treated with radiation therapy, 3,000 to 4,000 roentgens administrated over a period of 2 to 3 weeks, followed in 6 weeks by surgical excision of the tumor (Fig. 4).

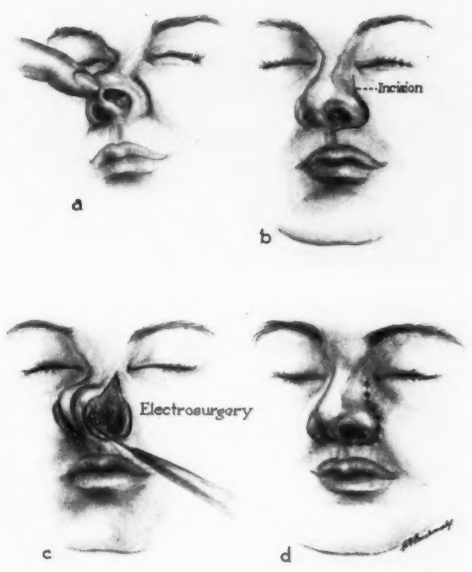


FIG. 3. a, Illustration of tumor involving nasal septum or turbinate bones. b, Lateral rhinotomy incision through ala of nares which extends as high in the nasolabial fold as desired. The ala of the nose is turned medially permitting small tumors to be removed from septum and turbinates. c, d, The tumor is thoroughly destroyed with electrocoagulation. The muscles and subcutaneous tissues are closed with fine interrupted chromic catgut. The skin is closed with interrupted mattress sutures of fine silk.

This technique permits both nares to be exposed.

Treatment of cancer of the paranasal sinuses. The methods of treatment of cancer of the paranasal sinuses are irradiation therapy and surgery. A substantial percentage of patients with cancer of the sinuses are observed in an advanced stage of the disease; the tumor having invaded one or more walls and extended into neighboring structures. There is infection with retained pus produced by blockage of the osteum into the nose. Even in advanced cases, cancerocidal amounts of irradiation therapy followed by radical surgery will destroy the cancer in many patients permitting them to live in good health and return to their various occupations.

A diagnosis is established by histologic study of representative tissue from the tu-

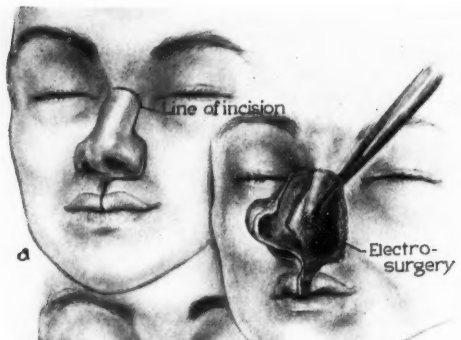


FIG. 4. For more extensive tumors of nasal fossa, an incision is made through the midline of the upper lip to the columella of the nose, extended around the ala in the nasolabial fold to a point below the medial canthus of the eye and across the bridge of the nose. This technique permits careful inspection of tumors involving the posterior nasal fossa and destruction with electrocoagulation. The muscles and subcutaneous tissues are closed with interrupted fine chromic catgut; the skin is closed with interrupted mattress sutures of fine silk.

mor; the extent it has invaded surrounding structures is determined by roentgenograms. If there is destruction of the orbital floor or invasion of the orbital contents, preservation of the eye is rather remote. Extension into the pterygoid fossa is difficult to determine until the tumor is adequately exposed.

Irradiation therapy. After the extent of the tumor is determined, roentgen therapy is administered through 2 or 3 ports varying in size from 4 to 6 centimeters: one directly over the tumor, one lateral, and occasionally a third intraoral. If there is involvement of the orbital contents or ethmoid and sphenoid cells a fourth or fifth port is administered; one through the zygoma just above the lateral port, and one straight through the orbit from the front. Treatment factors are: 260 kilovolts, 15 milliamperes, 0.5 millimeter of copper plus 1 millimeter of aluminum, 50 centimeters target skin distance, the dose varying from 2,400 to 3,000 roentgens through each port. Treatments are administered daily in doses of 300 roentgens which will result in epithelitis, desquamation, and occasionally blistering; these complications disappear after 4 to 6 weeks.

Surgery. Conservative surgery is not advisable in the treatment of cancer of the paranasal sinuses since it does not permit removal of sufficient tissue to effect a cure. It is my practice to resect the superior maxilla which frequently includes exenteration of the orbit. This procedure is performed through a Fergusson incision which reveals the extent of the tumor and permits exploration of surrounding structures, i.e., nasal cavity, nasopharynx, pterygoid fossa, ethmoid and sphenoid cells, and orbit.

Intratracheal anesthesia with the tube inserted through the mouth on the uninvolved side is the anesthesia of choice. The pharynx is carefully packed with a moist pack; pentothal sodium, oxygen, and nitrous oxide are used throughout the operation which permit the use of electrosurgical current.

The patient is placed on the operating table on his back with the head of the table lowered; the neck is slightly extended to facilitate drainage of secretions and blood from the respiratory tree. The external carotid artery and its branches are ligated at the beginning of the surgical procedure to reduce bleeding during and after the operation.

An incision is made through the upper lip in the midline to just beneath the columella of the nose, and extended around the ala in the nasolabial sulcus to the height desired. If the eye is to be preserved the incision extends to 2 centimeters below the inner canthus of the eye (Fig. 5), then follows the infraorbital ridge laterally beneath the border of the orbit with the concavity upward across the malar bone to a point above the zygomatic process.

When exenteration of the orbit is necessary the incision is extended to the level of

the eyebrow, then laterally along the supraorbital ridge above the zygomatic process. If the zygoma is involved the incision is extended to the anterior surface of the ear, downward in front of the auditory canal to the lobe, which permits exposure of the entire zygoma and surrounding tissues.

The incision is made with the electrosurgical current through the thickness of the lip and cheek to the bone throughout its entire length except in front of the ear. The infraorbital branch of the facial nerve which follows the upper border of the zygomatic arch is preserved if possible, to prevent paralysis of the lower half of the orbicularis muscle. The skin and soft tissues of the cheek except the subcutaneous fat are reflected from the maxilla except when the skin is involved over the growth, in which case it is removed with the growth and replaced later with a pedicle flap from the forehead or neck.

The mucous membrane in the gingival labial sulcus is severed with a scalpel; the mouth is opened widely and the central incisor tooth on the involved side is extracted; an incision is made in the midline of the hard palate with electrosurgical current backward to the soft palate, across the posterior edge of the hard palate to the superior alveolar tuberosity to meet the incision in the gingival labial sulcus. An incision is made through the midline of the palate and through the junction of the superior maxilla and nasal bones with chisel and hammer. The malar bone and zygoma are examined; any involved portion of the zygoma is removed with a Gigli saw. When the floor of the orbit and orbital contents are not involved the infraorbital ridge is preserved to prevent double vision and loss of function of the eye. Invasion of the infraorbital ridge and orbital contents requires exenteration of the eye.

The superior maxilla is removed with heavy bone forceps. The smaller blood vessels are clamped and coagulated with the electrocoagulator; larger vessels are ligated with fine chromic catgut.

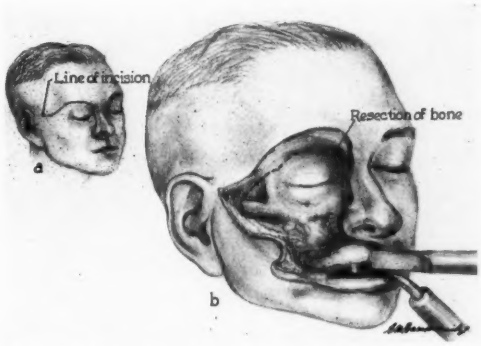


FIG. 5. a, Resection of maxilla and orbital contents. Incision is made through the midline of lip to columella of nose, around ala in nasolabial fold to eyebrow; cheek flap is turned back. b, With chisel and hammer, an incision is made through hard palate and maxilla; the zygoma is severed with Gigli saw.

If the cancer has invaded the ethmoid and sphenoid cells or pterygoid fossa, these areas are cleaned out with the electrocoagulator; the involved tissue is coagulated, curetted, and recoagulated until normal appearing tissue is found. Remnants of involved bone are treated likewise. Any areas that may contain residual cancer are treated with radium needles or tubes in rubber cots, a dosage calculated to give 6,000 to 10,000 roentgens at 1 centimeter depth being administered. The radium tubes or needles are attached to long silk sutures brought out through the most convenient angle of the wound.

A split thickness skin graft sufficiently large to cover all raw surfaces of the cheek, maxillary cavity, and orbit has improved permanent results of this operative procedure. The graft is trimmed and sutured in place with No. 0 chromic catgut (Fig. 6). A few catgut sutures are scattered throughout the graft to obliterate dead space beneath it. The cheek and lip flap is sutured back in the normal bed, the muscles and subcutaneous tissues are sutured with interrupted No. 0 chromic catgut; the skin is closed with interrupted sutures of fine black silk. The maxillary or orbital cavity is packed firmly with iodoform gauze to hold the skin graft

snugly and prevent postoperative oozing. A pressure dressing is placed over the cheek and held with an ace bandage.

Radical neck dissection. Carcinoma of the paranasal sinuses usually does not metastasize to the lymph nodes except in the advanced stage; consequently, radical neck dissection is not included with resection of the superior maxilla unless there is definite evidence of metastases. Two patients had metastases to the upper jugular chain of lymph nodes when first observed. Two other patients developed metastases to the upper jugular chain of nodes after 2 year and 3 year intervals. All 4 patients are living—one 2 years, one 3 years, two 4 years after radical neck dissection—with no clinical evidence of recurrence of their disease. Two other patients with extensive cancers of the antrum developed metastases to the lymph nodes in the parotid gland area. These patients were treated by implantation of low intensity radium needles in the parotid gland and jugular chain of nodes. One patient expired from generalized metastasis 1 year later; the other patient has remained well with no clinical evidence of recurrence for 3 years.

Postoperative care. Postoperative care consists of placing the patient in bed lying on the uninvolved side until he recovers sufficiently from the anesthesia to move normally. The following day the patient is encouraged to be out of bed. Warm, wet saline dressings reduce edema of soft tissues and assist in making the patient comfortable.

Nasal feedings, using an ordinary No. 18 French urethral catheter, are begun 24 hours following surgery and continued for a period of several days. The patient is taught to insert the nasal catheter himself. A high caloric and vitamin diet, up to 3,000 calories daily, takes care of the patient's nutritional needs. Hydrogen peroxide irrigations aid in removal of the gauze packs when the wound is dressed. It is irrigated with warm solutions of sodium chloride and sodium bicarbonate and the cavity is repacked with iodoform gauze.

If radium tubes and needles are used they are removed along with the iodoform gauze pack when the calculated dose of radium has been administered. If radium is not used, the gauze pack is removed at the end of 8 to 10 days.

A prosthesis, described previously,[1] which has already been prepared by a dental surgeon is inserted to permit the patient to eat, drink, and speak without difficulty.

DISCUSSION

The indications for enlarging the scope of treatment of cancer of the paranasal sinuses and more extensive malignant lesions of the nasal fossa are based on sound surgical principles. The primary method of extension is by direct invasion of surrounding tissues and to a lesser degree through the lymphatics and blood stream. The physiology of the nasal fossa and paranasal sinuses is not conducive to the embolization of cancer cells into the lymphatics or blood stream. In most patients, with the exception of those with cancers of the nasal septum and sphenoid and ethmoid cells, the disease remains unilateral and does not metastasize locally or extend below the clavicle until late in its course.

Preoperative irradiation therapy is used for the more extensive cancers of the nasal fossa and all cancers of the paranasal sinuses for the following reasons: The growths are active: the lymphatic channels and adjacent tissues are being invaded. Administration of cancerocidal irradiation therapy will destroy and devitalize a substantial amount of the tumor, block the lymphatic channels, and lessen the danger of dissemination of malignant cells during the operative procedure. In one-third of the patients who had radical resection of the maxilla or orbital contents following preoperative radiation therapy, no viable malignant cells were reported in the pathologic specimen.

Radiation therapy sufficient to eradicate cancer of the paranasal sinuses frequently produces permanent changes in the tissues, i.e., radio-osteonecrosis, sclerosis, obliterating endarteritis, and chronic osteomyelitis.

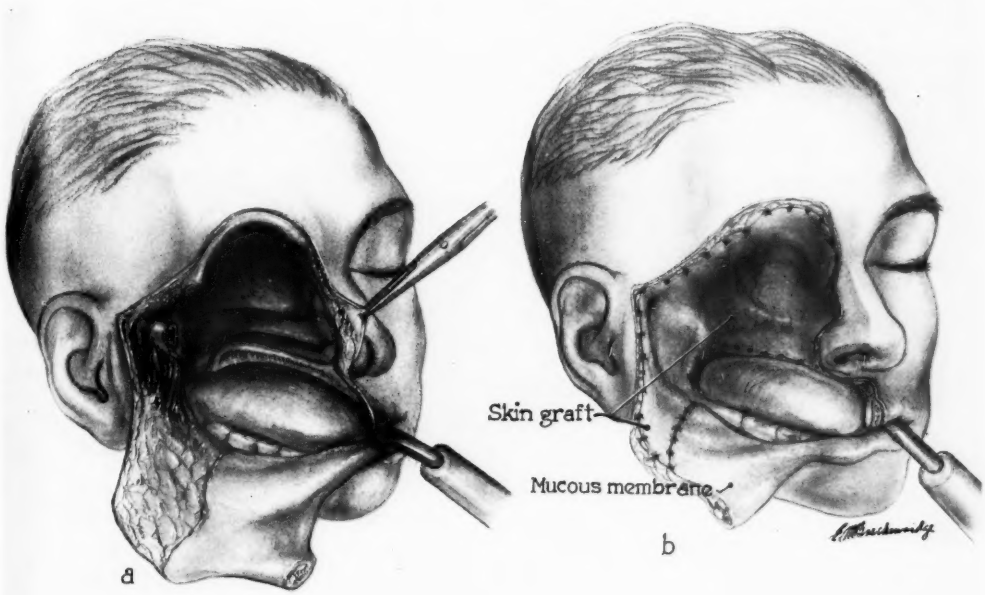


FIG. 6. a, Superior maxilla and orbital contents have been removed, b, The raw surfaces of the cheek flap and orbit are covered with split thickness skin graft. Cheek flap is resutured in place.

Surgical excision of the irradiated area, including a margin of healthy tissue, alleviates these complications and removes lingering cancer cells.

There were 64 patients with cancer of the paranasal sinuses. In 26 patients of this group the diagnosis was made relatively early; in 38 the disease was advanced, i.e., destruction of one or more sinus walls, extension into the soft tissues of the cheek, nasal cavity, orbit, or into the pterygoid fossa. Two patients refused all therapy after a histologic examination of the tissue had been made; in 2 patients the disease was too advanced to warrant any type of therapy.

Forty patients had irradiation therapy followed by radical surgery. Of these, 19 were operated upon from 3 to 6 years ago, and 21 from 1 month to 3 years ago. Of the 19 who were operated upon over 3 years ago, 14 are living and well and free of disease; 2 have died of recurrent cancer. One has been lost to follow-up and 2 died of unrelated disease. Twenty-one patients were operated upon from 1 month to 3 years ago.

Fifteen patients had irradiation therapy only. Ten of these have been followed for from 3 to 6 years. Six died of recurrent cancer, 2 are living and well but have complications of intensive radiation therapy, and 1 died of unrelated disease. Five patients who had radiation therapy only have been treated for from a few months to 3 years. For patients who have been treated for less than 3 years, no statistical material is given.

Of the 8 patients with cancer of the nasal fossa, 2 had lymphosarcoma, 1 lymphoepithelioma, and 1 myxosarcoma; 3 of these were observed in the advanced stage of the disease. All 4 were treated with intensive radiation therapy and have expired from the disease 1 to 3 years after the first observation. Two patients with squamous cell carcinoma, 1 with cylindroma, and 1 with malignant melanoma were treated by lateral rhinotomy incision and thorough removal

of the tumor with electrosurgery. These 4 patients have been followed for from 3 to 6 years and are clinically free of disease. The average postoperative stay in the hospital was 11 days. There was no operative mortality.

SUMMARY

A study of 72 malignant tumors of the paranasal sinuses and nasal fossa has been made. The nasal fossa is infrequently involved. Most of these cancers are of squamous cell origin. Radiosensitive tumors, i.e., lymphoepitheliomas, lymphosarcomas, and anaplastic carcinomas involving the nasal fossa, are treated with irradiation therapy. Tumors involving the paranasal sinuses are treated with irradiation therapy followed by radical resection of the superior maxilla with or without exenteration of the orbit. A well fitting prosthesis provides the patient with good functional and cosmetic results and with no difficulty in swallowing, phonation, or mastication.

THE RESULTS OF INTERRUPTION OF THE INFERIOR MESENTERIC ARTERY AND ITS BRANCHES IN THE RHESUS MONKEY

J. L. BRAITHWAITE, M.D., M.R.C.S., Liverpool, England

A PREVIOUS PAPER (5) described the effects of interruption of the inferior mesenteric artery and its branches at various sites and in different combinations on the terminal part of the large gut in the rat.

The results of these experiments were discussed in relationship to similar procedures recently carried out in man, although it was pointed out that there are differences in arterial pattern between the rat and man, particularly the absence of anastomotic arcades in the former. In order to confirm previous deductions, further complimentary experiments have been undertaken in a limited series of rhesus monkeys (Macaca mulatta) in which the arterial supply to the hindgut resembles more closely the human pattern. The evidence to be presented affords confirmatory support regarding the practicability of high ligation of the inferior mesenteric artery in selected cases in man. This is based on the similarity of arterial supply to the hindgut in the monkey and man, and the great reserve of the collateral circulation following ligation experiments of various types in the former.

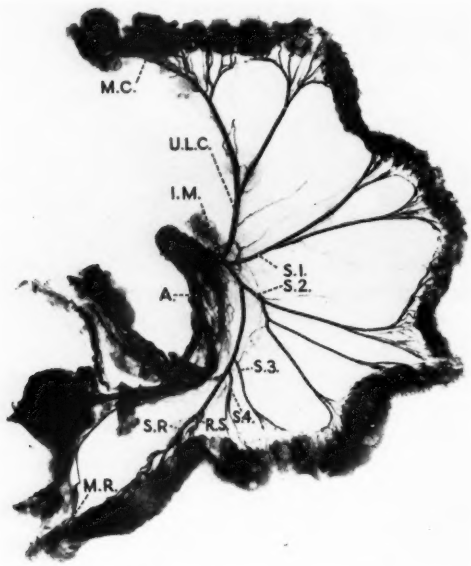
MATERIALS AND METHODS

The normal arterial arrangements have been studied in 3 animals and noted in a further 7 undergoing operation, whose weights ranged between 1.1 and 6.9 kilograms. Operations involving interruptions of the inferior mesenteric artery at various levels have been carried out. The larger branches of this vessel, such as the upper (ascending) left colic, inferior left colic (sigmoid), and superior rectal arteries have also been occluded in single instances and in 1 case the arcade system was interrupted over a limited area; in all instances double thread ligatures were used. Anesthesia was effected by intravenous nembutal.

The period of survival after operation varied between 10 and 16 days. This interval was based on previous experience of the time taken for the full development of a collateral circulation in other mammals (3, 4, 5). The animals were killed by an overdose of intravenous nembutal and injected through the thoracic aorta with a radiopaque medium (micropaque). The efficacy of the injection was determined by direct observations on the filling of the gut vessels after delivering a loop of gut through the original midline abdominal incision. The amount of medium introduced varied between 7 and 12 milliliters. Dissection was carried out in the area of the ligations to confirm the site of interruption and to note the macroscopic appearance of the adjacent vessels. Adhesions were common around the site of the thread ligatures and the freeing of adjacent viscera was a difficult procedure. A segment of the hindgut extending from a point well proximal to a point well distal of the site of interruption, together with its vascular pedicles, was removed. Arteriographs were taken of the specimen, and in certain instances small areas of gut were removed for microradiography to enable a comparison to be made between the intrinsic vessels on the gut wall in the zone operated upon and those in adjacent areas.

Enlarged positives of the arteriographs studied in conjunction with the specimen

From the Department of Anatomy, University of Liverpool, Liverpool, England. Aided in part by a grant from the Medical Research Council.



The following key is applicable to all the figures: *A.*, abdominal aorta; *I.M.*, inferior mesenteric artery; *I.R.*, inferior rectal artery; *M.*, marginal artery; *M.C.*, middle colic (branch of superior mesenteric) artery; *M.R.*, middle rectal artery; *R.S.*, rectosigmoid artery; *S.*, sigmoid artery; *S.R.*, superior rectal artery; *U.L.C.*, upper (ascending) left colic artery.

FIG. 1. Arteriograph of the vascular arrangements to the terminal part of the large gut in the normal animal. ×0.47.

facilitated an accurate assessment of the changes in vascular pattern.

ARTERIAL ARRANGEMENTS IN THE NORMAL ANIMAL

In addition to 3 observations in the rhesus monkey 2 additional studies have been made on other types of old-world monkeys, namely the sooty mangabey and the green monkey. The findings are essentially similar in all three species.

Inferior mesenteric artery. This vessel arises from the ventral aspect of the abdominal aorta, about 2 centimeters proximal to its bifurcation (Fig. 1). Its first branch is the upper (ascending) left colic artery, which coursing upward and to the left in the mesentery divides into two large branches, one anastomosing with the middle colic branch of the superior mesenteric artery, the other (descending branch) with an anastomotic branch of the proximal inferior left colic (first sigmoid) artery.

Inferior left colic (sigmoid) arteries. These branches vary in number between 4 and 7, although most frequently 5 are present. The first sigmoid artery frequently arises in common with the upper left colic artery, which incidentally is the most common arrangement (noted by Drummond and Steward and Rankin) in man. The bifurcation of these vessels together with the upper left colic artery and its anastomosis with the middle colic branch of the superior mesenteric artery forms a system of arcades from which the terminal arteriae rectae arise. Of the latter vessels, some are short and run only to the mesenteric border while others are longer and cross the gut wall to the antimesenteric border; the intrinsic anastomosis between them is, however, of limited extent (Fig. 2). The arrangement of the arteriae rectae and the limitation of their anastomoses corresponds closely to that described and illustrated by Ross in man.

Rectosigmoid branches. These vessels, much smaller in size than the sigmoid arteries and variable in number, arise from the inferior mesenteric artery immediately proximal to the bifurcation of its continuation, the superior rectal artery, into its main right and left branches, and supply the rectosigmoid junction; although linked by transverse communications (between themselves), they do not always anastomose with the lower division of the last sigmoid artery.

Superior rectal artery. This is the continuation of the inferior mesenteric artery. It divides in the region of the rectosigmoid junction into right and left branches which themselves divide and course in a longitudinal direction down the wall of the rectum. The terminal rami of these vessels become extremely tortuous in the lower rectum and have a corkscrew appearance.

Middle rectal artery. This is a constant vessel and is bilaterally disposed. It arises from

FIG. 2.

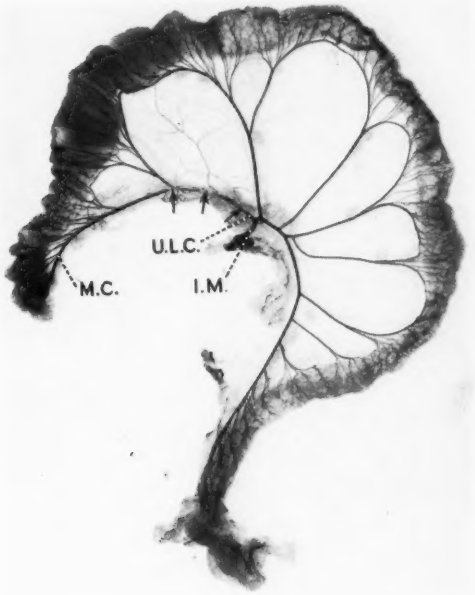


FIG. 3.

FIG. 2. Microarteriograph of the intrinsic vessels on the gut wall. ×3.3.

FIG. 3. Arteriograph showing interruption of the upper (ascending) left colic artery. The sites of occlusion are indicated by arrows. ×0.55.

the internal iliac artery by a trunk common to it and the inferior vesical artery (Fig. 1). The latter, after giving off a vesical contribution, is expended in the supply of the prostate gland. Multiplicity of the middle rectal artery has not been observed in the present series.

Inferior rectal artery. This is a small vessel arising from the internal pudendal artery and coursing inward to supply the anal canal and adjacent part of the rectum.

RESULTS OF THE LIGATION EXPERIMENTS

Interruption of upper left colic artery. Following interruption of this vessel at three sites along its course: (1) near its origin, (2) just proximal to its bifurcation, and (3) midway between these two points, the arcade spanning the ligated zone has undergone dilatation and constituted the most important collateral channel (Fig. 3). The small vessels in the mesenteric window are more prominent than those related to the other arcade systems and these are connected with small collateral networks which are situated around the interruption sites.

These small collateral plexuses are shown more clearly in the microarteriograph (Fig. 4).

Interruption of inferior mesenteric artery at an intermediate level. Figure 5 is an arteriograph taken after ligation of the inferior mesenteric artery between the origin of the second and third sigmoid branches. The appearances are similar to those described in Figure 3. The arcade which has a proximal contribution from the second sigmoid artery has undergone considerable enlargement. The small vessels in the windows of the mesentery are also more prominent than normally and there is a localized plexus of vessels around the site of ligation.

FIG. 4.

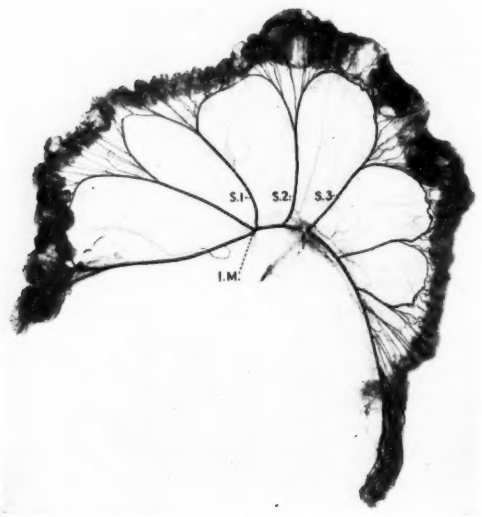


FIG. 5.

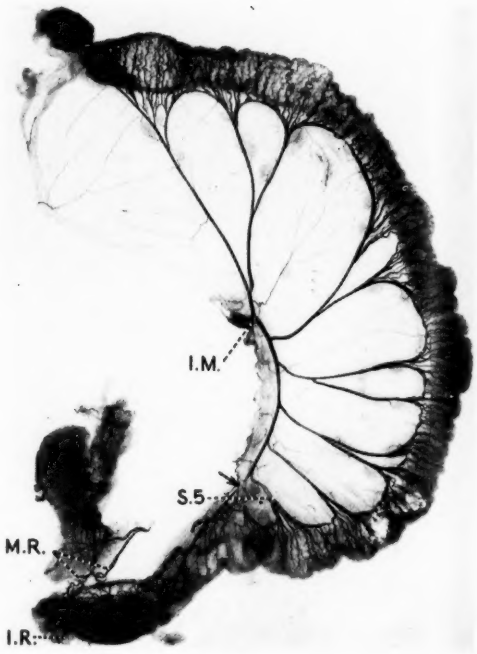


FIG. 6.

FIG. 4. Microarteriograph of the sites of ligation indicated in Figure 3. Note the small collateral channels which have developed around the occluded segments of the vessel. ×2.5.

FIG. 5. Arteriograph showing interruption of the inferior mesenteric artery at an intermediate level between the origins of the second and third sigmoid arteries. ×0.36.

FIG. 6. Arteriograph showing interruption of the inferior mesenteric artery at a low level. Note the ischemic zone on the antimesenteric border of the gut wall. ×0.57.

Interruption of inferior mesenteric artery at a low level (*Fig. 6*). This has been divided at a point distal to the origin of the last sigmoid artery (distal also to the last anastomotic arcade). There is a zone of ischemia about 1.5 centimeters in extent situated mainly on the antimesenteric border of the gut; proximal to this area the arteriae rectae appear normal. Retrograde filling of the superior rectal artery and its rectosigmoid branches has occurred and the rectum is well vascularized. The middle rectal pedicles are both considerably enlarged, and the anastomoses between these vessels and the branches of

FIG. 7. Microarteriograph of the same specimen as Figure 6, showing the site of interruption and the zone of ischemia ×2.7.

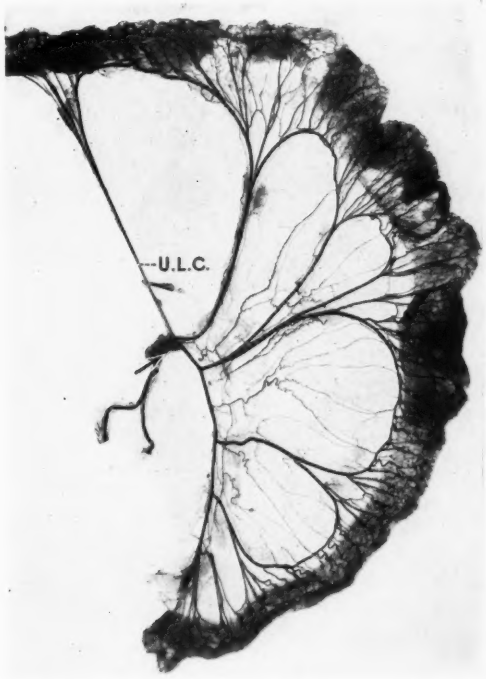


FIG. 8. Arteriograph showing interruption of the inferior mesenteric artery at its origin. The site of interruption is indicated by an arrow. ×0.51.

the superior rectal artery account for the maintenance of the arterial supply to the rectum.

The inferior rectal artery of one side is considerably dilated and its anastomoses with the lower branches of the superior rectal artery are evident.

The ischemic zone and the state of the adjacent vessels can be seen to better advantage in the accompanying microarteriograph (Fig. 7).

Interruption of the inferior mesenteric artery at its origin. The site of interruption is indicated by an arrow (Fig. 8). It is evident that all the hindgut vessels are well injected. The collateral circulation responsible for the complete vascularization has been afforded by the middle colic branch of the superior mesenteric artery and thence through the marginal anastomosis between this vessel and the upper left colic branch of the inferior mesenteric artery. The vessels in the mesenteric windows are enlarged and tortuous.

An arteriograph (Fig. 9) following interruption of the inferior mesenteric artery at its origin together with the proximal part of the upper left colic artery is similar. The middle colic artery is very much enlarged and the vessels in the mesenteric windows stand out prominently.

In both instances there was no marked enlargement of either the middle rectal or the inferior rectal arteries; this was probably because the supply from above was adequate to revascularize the whole area.

Interruption of sigmoid arteries. When 4 consecutive sigmoid arteries were ligated (Fig. 10) the collateral supply maintained the circulation to the area of gut deprived of its blood supply. The marginal artery stands out prominently and its caliber is much greater than that in the segment immediately proxi-

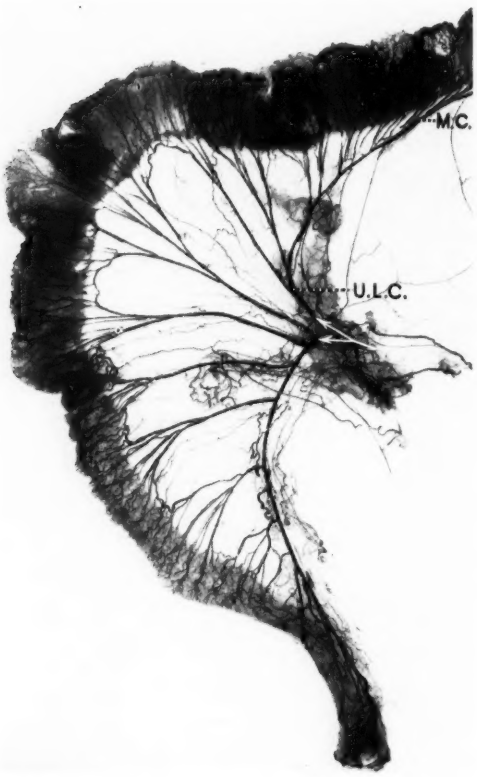


FIG. 9. Arteriograph showing interruption of the inferior mesenteric artery at its origin combined with occlusion of the proximal part of the upper left colic artery, seen from the posterior aspect. ×0.57.

mal and distal to the zone. The upper left colic artery is also dilated and there is an increased density of the small vessels in the window of the mesentery in the affected zone. The arteriae rectae arising from the convexity of the marginal vessels seem enlarged and more tortuous than normal vessels.

Interruption of arterial arcades. Figure 11 illustrates the effects of interruption of the arterial arcades. Three alternate arcades have been interrupted (*A*, *B*, *C*). In *A* the arcade together with its arteriae rectae has been divided. It will be seen that the vascularity of this area is not as well developed as in adjacent areas, although in the zone immediately proximal a few arteriae rectae show increased dilatation and tortuosity.

In *B* the arcade only has been divided leaving the arteriae rectae intact, and there has been a full compensation through the anastomoses between adjacent arteriae rectae, which themselves show a retrograde filling.

In *C*, a similar type of interruption to *A*, the zone is not as well vascularized as adjacent areas although there is some increased prominence of the arteriae rectae bordering on the zone. Further, a plexus of fine vessels in the window of the mesentery has increased in size and is reinforcing the blood supply to the mesenteric border of the gut by anastomoses with the intrinsic vessels.

DISCUSSION

These experiments demonstrate the great potentiality of the collateral circulation in the different types of occlusion. It is evident that if the marginal artery is intact there is no risk of impaired viability of the gut after ligation of the inferior mesenteric artery along any part of its course except at levels below the last anastomotic arcade. Further, its branches such as the upper left colic artery and sigmoid arteries can also be tied without any ensuing complication.

The collateral circulation in these procedures is afforded by the intact arcades which contribute to the marginal artery; additional to this source of supply, small collateral vessels around the ligation sites and the small vessels running in the mesenteric windows are less important features of the morphology of the collateral circulation.

When ligation is carried out below the last anastomotic arcade the gut caudal to this level is potentially dependent on two sources of supply: (1) from above, by the intrinsic anastomoses on the gut wall between branches from the more proximal arteriae rectae arising from distal arterial arcades on the one hand and those arteriae rectae arising from the rectosigmoid and superior rectal arteries on the other, and (2) from below, by the middle and inferior rectal arteries of both sides. It is clear from Figure 6 that both the middle and inferior rectal arteries are capa-

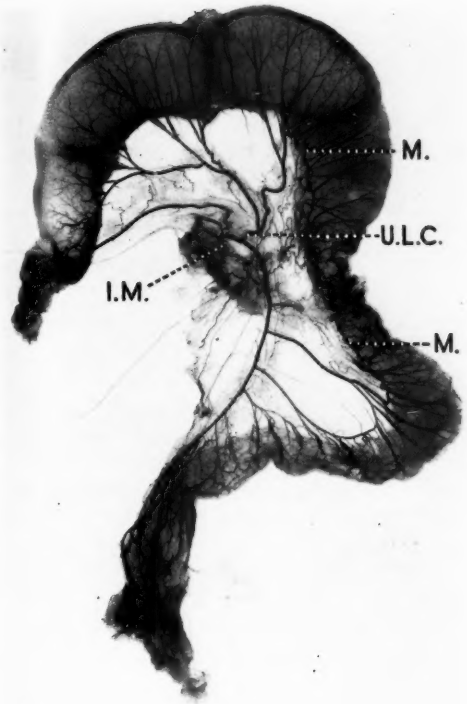


FIG. 10.

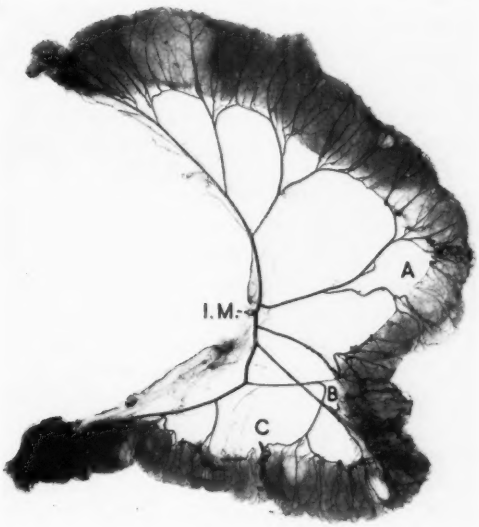


FIG. 11.

FIG. 10. Arteriograph showing interruption of 4 consecutive sigmoid arteries.

FIG. 11. Arteriograph showing interruption of arterial arcades. Three alternate arcades have been interrupted, indicated by *A*, *B*, and *C*. ×0.61.

ble of considerable dilatation and, by their anastomoses with the terminal branches of the superior rectal artery, have been responsible for the complete revascularization of the rectum. Although a small ischemic zone in the region of the rectosigmoid junction still remains, this has a normal histologic appearance. The potentiality of these caudal rectal vessels as collateral channels is similar in the rat and supports the findings of Ault, Castro, and Smith (1, 2), Goligher, and others in man, while refuting the opinion of Steward and Rankin that, in resection of the left colon in man, no rectal stump should be left because of the likelihood of necrosis if dependent for its blood supply on the middle and inferior rectal arteries only. The intrinsic anastomoses on the gut wall are, however, poorly developed (Figs. 2, 4, and 7) and in this respect show similar features to those described in man by Steward and Rankin and Ross though differing from the well developed lattice work of transverse and longitudinal anastomoses in the rat (5: Figs. 1 and 2); in the latter animal it is possible to interrupt the arterial tree at any level because these intrinsic anastomoses compensate in all instances for the temporary ischemia. Indeed the intrinsic anastomoses on the gut wall in the rat are comparable to the arterial arcades present in the monkey and man and are equally effective as collateral channels.

The results of the present experiments confirm in the main previous findings in the rat and afford confirmatory support for the rationale of ligation of the inferior mesenteric artery at its origin in selected cases in man. This procedure has been previously practiced in the course of radical operations for the extirpation of carcinomas of the rectosigmoid junction by Ault, Castro, and Smith, Goligher, Snellman, and others.

SUMMARY AND CONCLUSIONS

The arterial arrangements and the collateral circulation have been studied in the rhesus monkey.

Interruption of the inferior mesenteric artery at various levels and of its larger branches has been carried out in 7 animals. The resultant effect in all experiments except 1 has been a temporary ischemia later compensated by the collateral circulation. Ligation of the inferior mesenteric artery distal to the last arterial arcade presents an area of ischemia in the rectosigmoid area still present after 2 weeks.

The intrinsic anastomoses of vessels on the gut wall are inadequate to compensate fully for any major interruption of the arterial arcade and arteriae rectae arising therefrom.

The study affords additional support for ligation of the inferior mesenteric artery at its origin in selected cases in man.

REFERENCES

1. Ault, G. W., Castro, A. F., and Smith, R. S. Carcinoma of the upper rectum and rectosigmoid; clinical report on high inferior mesenteric ligation. Postgrad. M., 1950, 8: 176–183.
2. Idem. Clinical study of ligation of the inferior mesenteric artery in left colon resections. Surg. Gyn. Obst., 1952, 94: 223–228.
3. Braithwaite, J. L. The effects of ligation of the pelvic arteries on the viability of the urinary bladder and the sufficiency of the collateral circulation in the experimental animal. Brit. J. Surg., 1953, 40: 610-616.
4. Idem. The morphology of the collateral circulation subsequent to complete interruption of the abdominal aorta in the rat. J. Anat., Lond., 1954, 88: 204–211.
5. Idem. The effects of interruption of the inferior mesenteric artery and its branches on the blood supply of the terminal part of the large gut in the experimental animal. Surg. Gyn. Obst., 1955, 100: 521–531.
6. Drummond, H. The arterial supply of the rectum and of the pelvic colon. Brit. J. Surg., 1913, 1: 677–685.
7. Goligher, J. C. The blood supply to the sigmoid colon and rectum: with reference to the technique of rectal resection with restoration of continuity. Brit. J. Surg., 1949, 37: 157–162.
8. Ross, J. A. The surgical significance of the intestinal vascular patterns. Edinburgh M. J., 1950, 57: 572–579.
9. Snellman, Björn. High ligation of the inferior mesenteric artery in operations for carcinoma of the left colon and rectum. Acta chir. scand., 1953, 105: 364–375.
10. Steward, J. A., and Rankin, F. W. Blood supply of large intestine: its surgical considerations. Arch. Surg., 1933, 26: 842–891.

INTRAPERITONEAL ANTIBIOTIC ADMINISTRATION IN THE TREATMENT OF ACUTE BACTERIAL PERITONITIS

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THE RESULTS of intraperitoneal administration of oxytetracycline and neomycin in the therapy of experimental and clinical acute bacterial peritonitis have been reported previously by the author (4, 5, 6). The number of patients who have been treated by this method of antibiotic administration has increased since the original reports and the clinical results have been good. It is the purpose of this article to evaluate our total experience with intraperitoneal instillation of the antibiotics, oxytetracycline, neomycin, and tetracycline hydrochloride, and to compare the results obtained with oxytetracycline and neomycin.

Thirty-eight patients with acute diffuse peritonitis have been treated with antibiotics administered intraperitoneally postoperatively. Oxytetracycline was used in 20 patients and neomycin was used in the other 18 patients. These patients did not receive any antibiotics postoperatively other than one administered intraperitoneally. The antibiotic that was chosen for postoperative administration was instilled intraperitoneally through two small polyethylene catheters which were introduced into the peritoneal cavity at the time of operation through a 13 gauge needle that was placed through the abdominal wall under direct vision. The catheters were not brought out through the site of the incision. One catheter was directed into the pelvis along either the right or left lateral gutter and the other was directed over the right lobe of the liver to the region of the right subphrenic space. One gram of the antibiotic that was used was mixed with 500 milliliters of normal saline to provide a concentration of 2 milligrams per milliliter and 250 milliliters were instilled through each catheter at the time of operation. Following that, 125 milligrams of antibiotic in solution were instilled through each catheter every 6 hours for a maximum of 72 hours. The solution was allowed to run in at a rate of 80 to 100 drops per minute. All patients received 1 to 2 grams of the antibiotic daily for 1 to 3 days. The usual postoperative dose was 500 milligrams of antibiotic diluted in 250 milliliters of normal saline which was given every 6 hours.

Peritoneal fluid was obtained for culture at the time of operation and every 24 hours thereafter by aspiration through the catheters just prior to instillation of an antibiotic (6 hours following a previous dose). The first 5 milliliters were discarded and then fluid was obtained for culture. The peritoneal fluid and serum of many of the patients were assayed for antibiotic content. Samples were obtained for assay at different intervals following instillation of a dose of the antibiotic.

RESULTS

The intraperitoneal administration of tetracycline compounds has been found in this laboratory to be contraindicated. Nausea and vomiting were observed following experimental use of the ascorbic and citric acid compounds and intraperitoneal adhesion formation occurred following use of tetracycline hydrochloride albumin complex.

Oxytetracycline and neomycin have been found to be nontoxic when administered intraperitoneally for 72 hours in large doses (4, 5, 6). There have been no intraperitoneal

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TABLE I.—TREATMENT AND BACTERIOLOGIC STUDIES OF PATIENTS WITH PERITONITIS

Patient Age, yrs.	*Diagnosis Operation*	*Preop. antibiotic therapy* No. hrs. therapy begun preop.*	*Peritoneal culture at operation*	*Peritoneal culture after I.P. therapy.*	*I.P.* Antibiotic 1. Dose at op. 2. Dose after op. 3. Pain on admin.*	*Remarks*
F.B. 81	Perforated sigmoid colon due to carcinoma. Transverse colostomy	1,500,000 UAPP 200,000 UAP 2 gm. strep. 41 hours	S. albus, S. aureus, Strep. fecalis, C. welchii, E. coli, yeasts	E. coli	Oxytetracycline 1. 1 gm. 2. 500 mgm. 1 dose 3. No pain	Moribund at time of oper. Died 6 hrs. postop.
W.C. 66	Necrosis of ileum due to mesenteric thrombosis. Resection ileum	900,000 UAPP 300,000 UAP 3 gm. strep. 60 hours	S. albus, Strep. fecalis, C. welchii, paracolon	No growth	Oxytetracycline 1. 500 mgm. 2. 500 mgm. 2 doses 3. Mild pain	Died 18 hrs. postop. Autopsy showed occl. coronary arteries
C.J. 62	Perforation of transverse colon by catheter. Transverse colostomy	300,000 UAPP 1 gm. strep. 10 hours	S. albus, C. welchii, E. coli	No growth	Oxytetracycline 1. 1 gm. 2. 500 mgm. q.6 h.	Prolonged recovery with progressive improvement. Died suddenly on 34th postop. day, probably due to pulmonary embolus
R.A. 3	Acute perforated appendicitis. Appendectomy	1,700,000 UAP 500 mgm. strep. 17 hours	S. albus, Strep. fecalis, E. coli, P. aeruginosa	No growth	Oxytetracycline 1. 500 mgm. 2. 250 mgm. q.6 h. 8 doses 3. No pain	Uneventful recovery
E.C. 59	Perforated sigmoid diverticulum. Transverse colostomy	600,000 UAPP 1 gm. strep. 10 hours	Strep. fecalis, E. coli, paracolon	No growth	Oxytetracycline 1. 1 gm. 2. 500 mg. q.6 h. 8 doses 3. No pain	Uneventful recovery
D.W. 49	Perforation of ileum due to carcinoma. Closure of ileum	None	A. aerogenes, C. welchii, paracolon	No growth	Oxytetracycline 1. 1 gm. 2. 500 mgm. q.6 h. 12 doses 3. No pain	Uneventful recovery
J.C. 57	Perforated duodenal ulcer. Closure of ulcer	None	S. albus, Strep. viridans, Strep. fecalis, paracolon, yeasts	No growth	Oxytetracycline 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. No pain	Uneventful recovery
S.S. 11	Acute perforated appendicitis. Appendectomy	600,000 UAPP 500 mgm. strep. 8 hours	Strep. fecalis, A. aerogenes, P. aeruginosa, C. welchii	No growth	Oxytetracycline 1. 1 gm. 2. 400 mgm. q.6 h. 8 doses 3. No pain	Uneventful recovery
J.T. 32	Acute perforated appendicitis. Appendectomy	None	S. albus, E. coli	No growth	Oxytetracycline 1. 500 mgm. 2. 500 mgm. q.6 h. 8 doses 3. Pain	Uneventful recovery
L.E. 27	Perforated duodenal ulcer. Closure of ulcer	None	S. albus, yeasts	No growth	Oxytetracycline 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. Pain	Uneventful recovery
J.H. 36	Perforated duodenal ulcer. Closure of ulcer	None	No growth	No growth	Oxytetracycline 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. Pain	Uneventful recovery
V.T. 32	Perforated gastric ulcer. Subtotal gastrectomy and vagotomy	None	No growth	No growth	Oxytetracycline 1. 500 mg. 2. 500 mgm. q.6 h. 8 doses 3. No pain	Uneventful recovery
A.G. 36	Perforated duodenal ulcer. Closure of ulcer	300,000 UAPP 600,000 UAP 8½ hours	No growth	No growth	Oxytetracycline 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. Mild pain	Uneventful recovery

*UAPP—units aqueous procaine penicillin. UAP—units aqueous penicillin. Strep.—streptomycin. I.P.—intraperitoneal.

TABLE I.—TREATMENT AND BACTERIOLOGIC STUDIES OF PATIENTS WITH PERITONITIS—Continued

Patient Age, yrs.	*Diagnosis Operation*	*Preop. antibiotic therapy* No. hrs. therapy begun preop.*	*Peritoneal culture at operation*	*Peritoneal culture after I.P. therapy.*	*I.P.* Antibiotic 1. Dose at op. 2. Dose after op. 3. Pain on admin.*	*Remarks*
J.B. 11	Acute perforated appendicitis. Appendectomy	None	S. albus, Strep. fecalis, C. welchii, A. aerogenes	No growth	Oxytetracycline 1. 500 mgm. 2. 500 mgm. q.6 h. 8 doses 3. Pain	Uneventful recovery
D.M. 38	Acute perforated appendicitis. Appendectomy	600,000 UAPP 24 hours	A. aerogenes	No growth	Oxytetracycline 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. Pain	Uneventful recovery
J.K. 72	Perforated sigmoid colon due to carcinoma. Transverse colostomy	1,200,000 UAPP 2 gm. strep. 500 mgm. terra. 36 hours	S. albus, E. coli	No growth	Oxytetracycline 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. Pain	Uneventful recovery
J.O. 50	Acute perforated appendicitis. Appendectomy	300,000 UAPP 12 hours	S. albus, Strep. fecalis, paracolon, E. coli	E. coli	Oxytetracycline 1. 1 gm. 2. 500 mgm. q.6 h. 72 hours 3. Mild pain	Uneventful recovery
G.D. 50	Perforated gastric ulcer. Closure of ulcer	None	S. albus, Strep. viridans, diphtheroids, yeasts	No growth	Oxytetracycline 1. 1 gm. 2. 500 mgm. q.6 h. 48 hours 3. Pain	Uneventful recovery
M.O. 93	Perforated duodenal ulcer. Closure of ulcer	300,000 UAPP 1 gm. strep.	C. welchii	No growth	Oxytetracycline 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. Pain	Uneventful recovery
C.L. 47	Acute perforated appendicitis. Appendectomy	None	Beta hemol. strep., C. welchii, E. coli, paracolon	No growth	Oxytetracycline 1. 500 mgm. 2. 500 mgm. q.6 h. 8 doses 3. No pain	Uneventful recovery
W.D. 62	Perforated sigmoid colon due to carcinoma. Left colectomy	None	S. albus, Strep. fecalis, C. welchii, E. coli	No growth	Neomycin 1. 1 gm. 2. 500 mgm. q.6 h. 12 doses 3. No pain	Uneventful recovery until 15th postop. day when died suddenly. Autopsy showed pulmonary embolus
G.M. 56	Perforated sigmoid colon following sigmoidoscopy. Closure of sigmoid colon	None	Strep. fecalis, C. welchii, E. coli, paracolon	No growth	Neomycin 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. Mild pain	Pelvic abscess with spontaneous resolution
F.A. 31	Acute perforated appendicitis. Appendectomy	None	Strep. fecalis, E. coli	No growth	Neomycin 1. 1 gm. 2. 500 mgm. q.6 h. 12 doses 3. Mild pain	Pelvic abscess with spontaneous resolution
A.J. 41	Perforated duodenal ulcer. Closure of ulcer	None	S. albus, anaerobic strep., Strep. viridans, Strep. fecalis, yeasts	No growth	Neomycin 1. 1 gm. 2. 500 mgm. q.6 h. 10 doses 3. No pain	Wound abscess. Uneventful recovery
J.T. 57	Acute perforated appendicitis. Appendectomy	600,000 UAPP 1 gm. strep. 24 hours	S. albus, anaerobic strep., E. coli	No growth	Neomycin 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. Pain	Uneventful recovery
S.R.	Perforated gastric ulcer. Closure of ulcer	None	S. albus, beta hemol. strep.	No growth	Neomycin 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. No pain	Uneventful recovery

TABLE I.—TREATMENT AND BACTERIOLOGIC STUDIES OF PATIENTS WITH PERITONITIS—Continued

Patient Age, yrs.	*Diagnosis Operation*	*Preop. antibiotic therapy* No. hrs. therapy begun preop.*	*Peritoneal culture at operation*	*Peritoneal culture after I.P. therapy.*	*I.P.* Antibiotic 1. Dose at op. 2. Dose after op. 3. Pain on admin.*	*Remarks*
C.L. 67	Perforated gastric ulcer. Closure of ulcer	None	Anaerobic strep.	No growth	Neomcyin 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. No pain	Uneventful recovery
A.J. 42	Acute perforated appendicitis. Appendectomy	300,000 UAPP 500 mgm. strep. 12 hours	S. aureus, E. coli, paracolon	No growth	Neomycin 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. Mild pain	Wound abscess. Uneventful recovery
V.L. 40	Perforated ileum due to intestinal obstruction. Resection ileum	1,200,000 UAPP 300,000 UAP 1 gm. strep. 36 hours	S. aureus, Strep. fecalis, C. welchii, E. coli	No growth	Neomycin 1. 1 gm. 2. 500 mgm. q.6 h. 12 doses 3. No pain	Wound abscess. Uneventful recovery
B.N. 16	Acute perforated appendicitis. Appendectomy	1,200,000 UAPP 500 mgm. strep. 48 hours	Bacteroides	No growth	Neomycin 1. 500 mgm. 2. 500 mgm. q.6 h. 3. No pain	Pelvic abscess 7 weeks postop.; drained by posterior colpotomy. Also had wound abscess. Uneventful recovery after drainage of pelvic abscess
W.L. 44	Ruptured tubo-ovarian abscess. Salpingo-oophorectomy, appendectomy	None	No growth	No growth	Neomycin 1. 500 mgm. 2. 500 mgm. q.6 h. 12 doses 3. Mild pain	Uneventful recovery
W.M. 24	Acute perforated appendicitis. Appendectomy	None	No growth	No growth	Neomycin 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. No pain	Uneventful recovery
H.T. 66	Perforated gastric ulcer. Subtotal gastrectomy	None	No growth	No growth	Neomycin 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. No pain	Uneventful recovery
H.T. 38	Perforated duodenal ulcer. Subtotal gastrectomy and vagotomy	None	No growth	No growth	Neomycin 1. 1 gm. 2. 500 mgm. q.6 h. 8 doses 3. No pain	Uneventful recovery
W.W. 66	Perforated duodenal ulcer. Subtotal gastrectomy	None	No growth	No growth	Neomycin 1. 1. gm. 2. 500 mgm. q.6 h. 8 doses 3. No pain	Uneventful recovery
M.G. 47	Ruptured tubo-ovarian abscess. Incision and drainage of abscess	None	Bacteroides	No growth	Neomycin 1. 1 gm. 2. 500 mgm. q.6 h. 12 doses 3. No pain	Uneventful recovery
E.L. 56	Necrosis of ileum due to internal hernia. Resection ileum	None	S. albus, Strep. fecalis, E. coli, C. welchii	No growth	Neomycin 1. 1 gm. 2. 500 mgm. q.6 h. 12 doses 3. No pain	Uneventful recovery
W.C. 30	Acute perforated appendicitis. Appendectomy	None	Beta hemol., strep., P. aeruginosa, bacteroides	No growth	Neomycin 1. 1 gm. 2. 500 mgm. q.6 h. 12 doses 3. No pain	Wound abscess. Uneventful recovery

adhesions, indications of chemical irritation, interferences with wound healing, or detrimental effects observed in patients during observation periods of 2 to 24 months following intraperitoneal instillations of these antibiotics in a concentration of 2 milligrams per milliliter.

A summary of the treatment and bacteriologic studies of the patients who have received intraperitoneal antibiotic therapy is shown in Table I. Each of the patients had severe diffuse peritonitis. One or more organisms were cultured from peritoneal fluid obtained at the time of operation of 30 patients, despite the fact that preoperatively 14 of these patients had received large quantities of antibiotics intramuscularly. On the other hand, a positive peritoneal culture was obtained postoperatively in only 1 patient following the institution of intraperitoneal antibiotic therapy. In that instance, 6 organisms were cultured at the time of operation, but only 1 organism, Escherichia coli, was cultured from peritoneal fluid obtained at autopsy. The patient received 2 doses of oxytetracycline intraperitoneally between the time of operation and death.

There were 4 deaths in this series, 3 of which were not thought to be due to peritoneal infection. Two of these deaths were due to a pulmonary embolus and 1 was due to a complete occlusion of both coronary arteries. The other patient, who is the first patient listed in Table I, was almost moribund at the time of operation and never completely reacted following the operation. There were 2 patients who developed clinical signs and symptoms of a pelvic abscess postoperatively and 1 patient in whom the presence of a pelvic abscess was proved. In the former 2 patients, there was rapid complete recovery, probably following spontaneous rupture of the abscess into the gastrointestinal tract; in the latter patient, there was rapid recovery following drainage of the abscess by a posterior colpotomy. Five patients in this series developed postoperative wound abscesses; the wound healed completely following drainage in each instance. Subcutaneous drains were not placed in these wounds at the time of the original operations. It is believed that these wound abscesses probably would have been avoided if drains had been employed postoperatively.

DISCUSSION

It is believed that the clinical results of treating these patients were good. There were no subphrenic or subhepatic abscesses in this series and, of the 3 pelvic abscesses, only 1 necessitated definitive surgical treatment. It should be emphasized that all of these patients had diffuse pyogenic peritonitis and that intraperitoneal oxytetracycline or neomycin was the only antibiotic employed postoperatively. The fact that cultures of peritoneal fluid obtained at operation were positive despite fairly intensive preoperative intramuscular antibiotic therapy in many instances but were negative following the intraperitoneal administration of an antibiotic, we believe, indicates that the latter route of administration is more effective in sterilizing the peritoneal cavity in cases of peritonitis.

Eleven of the 20 patients who were given oxytetracycline intraperitoneally experienced varying degrees of discomfort at the time of administration. The discomfort varied in intensity from a sensation of bloating to one of burning pain. Five of the 18 patients who received intraperitoneal neomycin experienced some discomfort at the time of instillation but the discomfort was never severe enough to necessitate cessation of administration. Neomycin instilled intraperitoneally caused less discomfort than oxytetracycline. Many of the patients who complained of discomfort at the time of neomycin administration were given a few milliliters of the same concentration of oxytetracycline solution just before termination of therapy. All of these patients expressed more pain at the time of administration of oxytetracycline.

The oxytetracycline and neomycin levels occurring in the peritoneal fluid and serum of patients are shown in Figures 1 and 2. The range of peritoneal fluid levels is shown

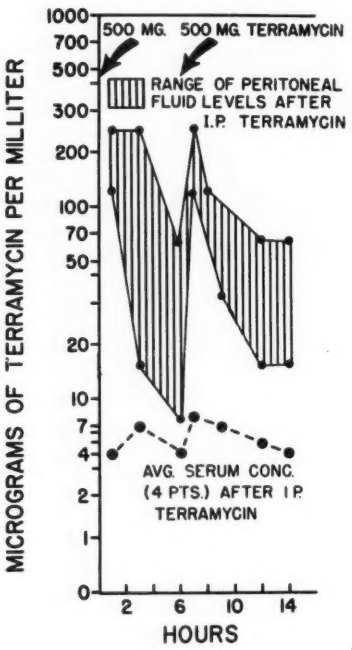

FIG. 1.

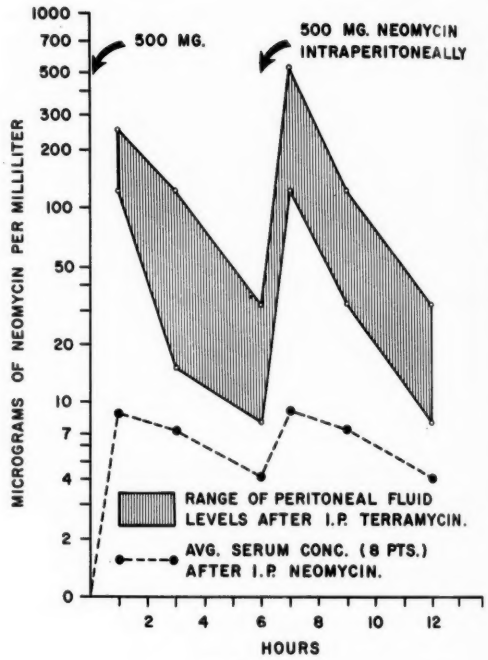

FIG. 2.

FIG. 1. Peritoneal fluid and serum oxytetracycline levels in 4 patients who received intraperitoneal oxytetracycline.

FIG. 2. Peritoneal fluid and serum neomycin levels in 8 patients who received intraperitoneal neomycin.

in order to demonstrate the extremes of the values obtained. It can be seen by comparison that there is little difference in the range of peritoneal fluid oxytetracycline and neomycin levels following administration of equal doses of the antibiotics intraperitoneally. There is little appreciable difference in the average serum concentrations following intraperitoneal administration of the two antibiotics. The significant finding is that the intraperitoneal method of parenteral administration results in high peak levels of antibiotic in the peritoneal cavity and slightly lower serum levels than are usually obtained by intravenous administration of the antibiotic. In contrast, the peritoneal fluid oxytetracycline level is the same as the serum level after intravenous administration of the antibiotic and no elevated peak levels are attained (4). Peritoneal fluid levels as high as 512 micrograms per milliliter can be obtained within 1 hour after administration of 500 milligrams of oxytetracycline or neomycin intraperitoneally, and levels as high as 64 micrograms per milliliter can be maintained for the following 6 hours.

It was shown in a previous study that fluid instilled through catheters left in the peritoneal cavity as long as 72 hours diffuses rapidly throughout the peritoneal cavity (6). Narat and co-workers have shown (2,3) that there is no mechanical interference with the intraperitoneal drip in animals or patients when tubes are left in the peritoneal cavity for several days. It is believed that the high peak levels of the antibiotics in the peritoneal fluid that occurred following the intraperitoneal administration of each dose and diffusion of the antibiotic were responsible for sterilization of the peritoneal cavity

in each of these cases. Correlation of the results of treating the patients in this series with the peritoneal fluid antibiotic levels suggests that therapeutic attempts at effective sterilization of the peritoneal cavity are all-important in the treatment of peritonitis, and that perhaps attempted sterilization of the blood stream is of secondary importance. This concept is in keeping with the experimental findings of Steinberg and Goldblatt (7), who demonstrated that retention of bacteria in the peritoneal cavity is associated with death of an animal, whereas rapid diffusion through the cavity and passage of bacteria into the blood stream are associated with survival. It was shown by these investigators (8) and by Beeson and his associates that the peripheral blood and reticuloendothelial system possess adequate bactericidal powers.

Although the 3 pelvic abscesses which did occur in this series were in patients who received neomycin intraperitoneally, it is not believed that this fact suggests a greater efficacy of oxytetracycline. It is more likely that these abscesses were contributed to by conditions present in these patients at the time of surgery. One patient who developed a pelvic abscess following perforation of the sigmoid colon had previous irradiation of her pelvis for carcinoma of the cervix. Another patient had a 3 day history compatible with acute appendicitis with perforation at the time that she came to the hospital, and there was localization of necrotic and purulent material in several areas of the pelvis at the time of operation.

Since there is little difference in the average peritoneal fluid concentrations and high peak levels occur following intraperitoneal administration of both antibiotics, neomycin is considered the drug of choice for intraperitoneal instillation because there is almost no pain associated with its administration. It has been shown experimentally and clinically in a previous study that neomycin is not a toxic drug when it is administered intraperitoneally for 72 hours in large doses (5).

Normal saline or Ringer's lactate solution is used as a diluent to obtain the desired concentration of 2 milligrams per milliliter of neomycin for intraperitoneal administration because it has been shown that the intraperitoneal injection of hypertonic solutions or isotonic solutions low in, or devoid of, inorganic electrolytes leads to marked shifts in body water and electrolytes, with an increase in peritoneal fluid volume and a decrease in plasma volume.

A 7.7 per cent incidence of pelvic abscess represents the only significant morbidity in this series of patients, each of whom had *diffuse* peritonitis demonstrated at the time of operation. These results are encouraging and it is believed that intraperitoneal instillation is the most effective method of administering an antibiotic in the treatment of acute bacterial peritonitis. The intraperitoneal instillation of neomycin, as outlined in this paper, is believed to be the most effective method of administration.

SUMMARY

1. Thirty-eight patients with acute diffuse peritonitis demonstrated at the time of operation have been treated postoperatively with the intraperitoneal administration of oxytetracycline or neomycin. There were no antibiotics employed postoperatively other than oxytetracycline or neomycin instilled intraperitoneally.

2. One or more organisms were cultured from peritoneal fluid obtained at the time of operation of 30 patients, despite the fact that preoperatively 14 of these patients had received large quantities of antibiotics intramuscularly. On the other hand, a positive peritoneal culture was obtained postoperatively in only 1 patient following the institution of intraperitoneal antibiotic therapy.

3. It is believed that the markedly high levels of oxytetracycline and neomycin in the peritoneal fluid that occurred following the intraperitoneal administration of each dose and diffusion of the antibiotic were responsible for sterilization of the peritoneal cavity in each of these cases.

4. Three of the patients in this series developed a pelvic abscess during their postoperative course; this 7.7 per cent incidence represents the only significant morbidity in this group of patients. Only 1 of these patients had a proved pelvic abscess; the other 2 patients developed clinical signs and symptoms consistent with an abscess. There were 4 deaths in this series. Two of these deaths were due to a pulmonary embolus and 1 was due to a complete occlusion of both coronary arteries. The other patient was almost moribund at the time of operation and never completely reacted following operation.

5. The intraperitoneal instillation of tetracycline hydrochloride is contraindicated because of nausea, vomiting, and intraperitoneal adhesion formation following administration.

6. There is little difference in the average peritoneal fluid and serum oxytetracycline and neomycin levels following administration of equal doses of the antibiotics intraperitoneally.

7. The intraperitoneal administration of oxytetracycline or neomycin is effective in treating patients with peritonitis. Intraperitoneal instillation of neomycin causes less discomfort than intraperitoneal instillation of oxytetracycline. Neomycin is considered the drug of choice for intraperitoneal administration.

REFERENCES

1. Beeson, P. B., Brannon, E. S., and Warren, J. V. Observations on the sites of removal of bacteria from the blood in patients with bacterial endocarditis. J. Exp. M., 1945, 81: 9.
2. Narat, J. K., and Carton, A. K. Intraperitoneal drip after laparotomies. Arch. Surg., 1951, 62: 520.
3. Narat, J. K., Cipolla, A. F., Cangelosi, J. P., and Vincenti, A. L. Intraperitoneal drip in presence of abdominal infection. Am. J. Surg., 1950, 79: 439.
4. Schatten, W. E., and Abbott, W. E. Intraperitoneal administration of terramycin in the treatment of experimental peritonitis. Surg. Gyn. Obst., 1953, 97: 445.
5. Schatten, W. E., DeSanctis, A. L., and Abbott, W. E. Intraperitoneal administration of neomycin in the treatment of peritonitis: experimental and clinical observations. Antibiotics Annual, 1954–1955. New York: Medical Encyclopedia, Inc.
6. Schatten, W. E., DesPrez, J. D., Cline, T. N., and Abbott, W. E. Intraperitoneal administration of terramycin in the treatment of acute bacterial peritonitis. Surgical Forum 1953, American College of Surgeons. Philadelphia and London: W. B. Saunders Co., 1954.
7. Steinberg, B., and Goldblatt, H. Studies on peritonitis; passage of bacteria from the peritoneal cavity into lymph and blood. Arch. Int. M., 1927, 39: 449.
8. Steinberg, B., and Martin, R. A. Diffusion and localization of experimental infections of the peritoneum. Surg. Gyn. Obst., 1944, 79: 457.

PALLIATION OF OVARIAN CARCINOMA WITH PHOSPHORAMIDE DRUGS

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OVARIAN CARCINOMA ranks fifth as cause of death from cancer in women in the United States, although, as pointed out by Ackerman and del Regato, only 15 per cent of all pelvic cancers are ovarian in origin. The insidious onset and course of this disease frequently delay diagnosis and therapy until distant metastases have occurred. Operation on ovarian tumors is often rendered difficult by extensive adhesions more or less fixed to the intestine, the bladder, and the pelvic wall. In spite of postoperative treatment with irradiation, the majority of these patients rapidly develop abdominal metastases which bring about death within a short time.

Various attempts to correct this serious situation have been made. Kottmeier reports notable improvement in prognosis by preoperative irradiation and surgery in the roentgen edema stage. Preoperative irradiation is recommended in all cases in which the patient is over 45 to 50 years of age and in which the occurrence of an ovarian tumor cannot be ruled out. Steroid hormone therapy as a palliative measure has been recommended and its rationale has been reviewed by Griboff. Chemotherapy with polyfunctioning alkylating agents such as nitrogen mustard and triethylene melamine has been employed in far advanced ovarian carcinoma with subjective and objective response in some cases.

The present article is a preliminary report concerning the observations on a group of patients who were treated with two related compounds N-N′-N″ triethylene thiophosphoramide and N-3 (oxapentamethylene) N-N′ diethylene phosphoramide.

Aided by a grant from the Lederle Laboratories Division of the American Cyanamid Co.

Twenty-two patients are included in this study (Table I). They ranged in age from 31 to 77 years, with an average age of 54 years. In all cases diagnosis was made by histopathologic examination of material obtained by biopsy or resection of tumor. The widespread nature of disease in these patients is apparent in Table I.

Previous therapy included: in the group in which surgery alone was performed, biopsy only in 1 case, exploratory operation and biopsy in 4 cases, resection of tumor in 7 cases; in the group in which surgery was followed by irradiation, exploratory operation in 1 case, resection of tumor in 7 cases; and 2 cases in which surgery was supplemented by both irradiation and hormone treatment.

Because pulmonary metastases were demonstrated by x-ray examination 1 patient had biopsy of a neck node only; diagnosis was verified at postmortem examination. In 5 cases, surgery was limited to abdominal exploration and biopsy of a tumor nodule. Resection of disease was undertaken in 16 patients. Eight individuals had 2 or more operations for the disease. Both ovaries were involved by cancer in 8 cases.

Triethylene thiophosphoramide was prepared in a solution containing 10 milligrams of drug per cubic centimeter of nonpyrogenic water. Sterilization was achieved by filtration and the solution was stored at 4 degrees C. Patients were treated at intervals of 1 to 3 weeks except in a few instances when the drug was administered intravenously every day for 3 to 5 days after which the longer intervals were employed. The total amount of triethylene thiophosphoramide given ranged from 110 to 780 milligrams (average 353 milligrams) in periods of 1 to

TABLE I.—SUMMARY OF CASES

Case Name Age, yrs.	Diagnosis	Present illness	Past treatment	Drug*	Total dose, mgm.	Route	Dates	Improvement	Duration, mos.	Side effects	Survival, mos.	Remarks
1 EB 39	Serous cystadenocarcinoma, bil. met. to omentum. Ovaries fixed in pelvis	Menstrual irregularities many yrs. Hormone therapy 1947. Intermittent abd. swelling many yrs.	June '54 Resection "pancake" omentum	T O	40 55 500 60	Into tumor I.V. Transvag. Transvag.	6-11-54 7-1 to 8-26-54 9-13-54 to 9-16-55 12-30-54	Disappearance tumor masses	16	None	16	Ovarian tumors injected at surgery. Pt. working
2 RC 54	Serous cystadenocarcinoma, bil. met. to breast, axillary nodes	Increase size abd. Breast lump	Apr. '53, salpingo-oophorectomy, subtotal hyster. May '53, postop. irradiation. Oct. '54, paracentesis —ca. cells	T 	460 25 60	Transvag. Breast nodule Transabd.	11-8-54 to 9-7-55 11-24-54 7-26-55 to 8-19-55	Control ascites. Disappearance breast lump	11	Anemia	11	Biopsy breast nodule showed carcinoma consistent with ovarian primary. Working as nurse
3 LD 41	Pseudomucinous cystadenocarcinoma, lt. ovary mass 12×15 cm. met. to omentum, mesentery, liver, small and large bowel	Catching RUQ pain	Mar. '55, exp. lap. Biopsy omentum	T O	385 40	Transabd. Transabd.	4-8 to 9-16-55 4-21-55	Decrease size abd. masses	6	None	6	Teaching full time and caring for 2 children
4 MF 31	Papillary adenocarcinoma bil. met. to uterus, tubes, rectosigmoid, bladder	Inc. abd. discomfort and swelling 3 yrs. duration	July '54, exp. lap. Postop. irradiation	T	210 260	Transabd. Transvag.	5-2 to 9-12-55 5-20 to 8-24-55	None	5	Pelvic abscess	5	Ambulatory. Continued ascites
5 PM 70	Pseudomucinous cystadenocarcinoma met. to supraclavicular nodes and lungs	Bil. neck nodules, cough, hemoptysis, multiple pulmonary nodules (x-ray)	Jan. '45, bil. salpingo-oophorectomy, huge ovarian cyst. Jan. '54, exc. biopsy supraclavicular mass. Irradiation to neck. 11-54 to 2-55, testosterone	T	385	Supraclavicular nodes	5-4 to 9-7-55	Decrease masses	5	WBC ↓ 1650	5	Continues work full time
6 PMcB 42	Serous cystadenocarcinoma bil. met. to omentum, liver, uterus, pleura	Recurrent pelvic mass. Pleural effusion. Abd. pain	Dec. '53, bil. oophorectomy, resection omentum	T O	193 285 160	Transabd. Transvag. Transvag.	7-8 to 9-11-55 12-11-54 to 7-8-55 1-3 to 1-28-55	Control pleural effusion. Temp. disappearance masses	7	Anemia WBC ↓ 1050	11	Continued work full time as nurse for 8 mos. then downhill course
7 HN 55	Papillary adenocarcinoma bil. met. to omentum	Lower abd. and pelvic pain	June '54, bil. oophorectomy and hysterectomy, residual disease	T	435	Transvag.	6-24-54 to 8-25-55	Disappearance mass	16	None	16	Continues housework
				T	100	I.V.	12-7-53 to 6-11-54	Disappearance dysuria and	22	WBC ↓ 1000	22	Normal activity

8 MP 71	Papillary adenocarcinoma met. to ureters and [illegible]	Int. obstruction, dysuria, recurrent pelvic mass	Dec. '52, lap. Apr. '53, lysis adhesions, radon seeds. Dec. '53, colostomy	T O	100 360 60 30	I.V. Transvag. Tumor nodules Transvag.	12-7-53 to 6-11-54 8-27-54 to 9-14-55 4-22 to 8-24-55 1-3-55	Disappearance dysuria and pelvic mass	22	WBC ↓ 1000	22	Normal activity
9 EVW 53	Papillary adenocarcinoma. Abd. "full of tumor," omentum studded	Abd. swelling, constipation, weakness, pleural effusion	Dec. '54, exp. lap. biopsy omentum	T O	520 50 20 10	Transabd. Transvag. I.V. Transabd.	2-10-55 to 9-19-55 2-15 to 8-11-55 3-12-55 4-4-55	Decrease masses. Control pleural effusion	8	Mod. anemia WBC ↓ 1350	8	Near normal activity
10 PC	Malignant dysgerminoma, met. to mesentery, omentum and bowel	Abd. swelling, pelvic tumor	Oct. '53, rt. salpingo-oophorectomy. Dec. '53, lt. salpingo-oophorectomy. Aug. '54, bowel resection, large mass fixed to rectum and bladder untouched	T O	780 140	Transvag. Transvag.	9-1-54 to 8-30-55 1-4-55 to 8-2-55	Disappearance pelvic mass	13	Anemia	13	Normal activity –
11 **BD** 62	Undifferentiated carcinoma, met. to mesentery and sigmoid	Recurrent pelvic mass	Oct. '53, hysterectomy. Postop. irradiation	T	215	Transvag.	4-29 to 9-29-54	Decrease abd. mass	3	None	6	Expired. CVA.
12 GE 65	Papillary adenocarcinoma met. to bowel and omentum	Abd. masses. Int. obstruction	Apr. '54, exp. lap. Postop. irrad. Sept. '54, int. resection	T	50 193	I.V. Transabd.	9-15 to 9-23-54 9-24 to 11-30-54	Sl. temporary decrease masses	1	WBC ↓ 1950	3	Expired. Intestinal obstruction
13 LF 77	Serous cystadenocarcinoma met. to "pelvic floor"	Abd. swelling	Feb. '54, exp. lap. for intra-abdominal hemorrhage. May '54 resection mass residual tumor	T	40 70 20	Into tumor Transvag. I.V.	5-29-54 9-2 to 9-7-54 6-8 to 6-9-54	None		None	4	Tumor injected during surgery. Expired. CVA
14 MJ 60	Papillary adenocarcinoma bil. met. to omentum and pleura	Ascites, pleural effusion, abd. masses	Apr. '54, exp. lap.	T	40 30 20 20	Transvag. Intraperit. Intrapleural I.V.	5-17-54 5-19-54 6-21-54 5-27 to 6-19-54	Decrease ascites	1	WBC ↓ 1450	1	Expired, pulmonary embolus
15 BK 69	Papillary adenocarcinoma, met. to inguinal and supraclavicular nodes	Left neck mass	1950, hysterectomy left oophorectomy, bilateral salpingectomy. Sept. '51, biopsy ing. node. Stilbestrol. 1952, bil. groin dissection	T	160	Into tumor	3-9 to 12-27-54	Regression mass	11	WBC ↓ 1650	11	Lost to follow-up

*T—N-N′-N″ triethylene thiophosphoramide
O—N-3 (oxapentamethylene) N-N′ diethylene phosphoramide

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TABLE I.—SUMMARY OF CASES—Continued

Case Name Age, yrs.	Diagnosis	Present illness	Past treatment	Drug*	Total dose, mgm.	Route	Dates	Improvement	Duration, mos.	Side effects	Survival, mos.	Remarks
16 MM 64	Pseudomucinous cystadenocarcinoma met. to pleura and throughout abd.	Abd. swelling, pain, recurrent ascites, nausea and vomiting	May '53, hysterectomy, rt. oophorectomy, postop. irradiation	T T	90 70	Intraperit. Transvag.	3-17 to 4-29-54 5-13 to 5-29-54	Decrease ascites and nausea	1	WBC ↓ 1000	3	Expired. Intestinal obstruction
17 CM 39	Serous cystadenocarcinoma bil. met. to omentum, peritoneum, liver, kidneys, uterus, sigmoid	Abd. discomfort	Sept. '54, oophorectomy, colostomy	T O	200 40	Transabd. Transabd.	9-24-54 to 12-1-54 12-15-54 to 12-29-54	None		None	3	Lost to follow-up
18 LN 71	Undifferentiated carcinoma met. to supraclavicular node, lungs, omentum, liver, bowel	Abd. distention and discomfort. Fever	Feb. '54, biopsy neck node	T	140 15 70	Transvag. Neck node. I.V.	4-6 to 5-14-54 4-23-54 4-8 to 4-21-54	None		WBC ↓ 1400	1½	Expired. Intestinal obstruction, uremia
19 FN 55	Papillary adenocarcinoma Gr. III met. throughout abdomen	Asymptomatic. Ca discovered at 1st operation. Subsequent symptoms of int. obst.	Sept. '49, hysterectomy, bil. salpingo-oophorectomy. Mar. '54, exp. lap.	T O	80 100 200 70	I.V. Transvag. Transabd. Transvag.	4-23 to 7-13-54 9-9-54 to 1-25-55 5-7-54 to 1-17-55 12-31-54	Minimal temporary regression abd. masses	3	None	10	Expired, intestinal obstruction
20 RR 36	Malignant dysgerminoma	Abd. swelling, pain	Apr. '54, exp. lap. Postop. irradiation. Aug. '54, partial resection abd. tumor	T	70 115	I.V. Transabd.	9-14 to 9-29-54 10-11-54 to 11-5-54	None		None	2	Expired. Intestinal obstruction
21 MS 52	Papillary adenocarcinoma bil. met. to pleura	Chest pain, abd. discomfort, pleural effusion	Dec. '53, hysterectomy	T	70 50 70 40	I.V. Intrapleural Transvag. Transabd.	1-27 to 9-14-54 2-2 to 3-18-54 5-7 to 7-30-54 9-11-54	Control pleural effusion	7	None	10	Aug. '54, int. anastomosis. Expired intestinal obstruction
22 IT 65	Serous cystadenocarcinoma bil. met. to pleura, liver, omentum, bowel	Abd. swelling and discomfort	June '52, lt. oophorectomy. Oct. '52, rt. oophorectomy. Nov. '52 to Jan. '53, irradiation	T	80 40 110 100 15	I.V. Intraperit. Intrapleural Transabd. Intrapericardial	11-25-53 to 2-12-54 2-19-54 to 9-9-54 3-5-54 to 9-2-54 3-11-54 to 7-15-54 8-19-54	Temporary control pleural, peritoneal, and pericardial effusion	7	WBC ↓ 1750	10	Normal activity as housewife 7 months. Expired intestinal obstr.

*T—N-N′-N″ triethylene thiophosphoramide
O—N-3 (oxapentamethylene) N-N′ phosphoramide

22 months (average 7.6 months). Due to a temporary shortage of drug and in order not to interrupt therapy oxapentamethylene diethylene phosphoramide was substituted for 1 to 3 doses of 10 to 70 milligrams in 8 cases. Oxapentamethylene diethylene phosphoramide was prepared in the same way as triethylene thiophosphoramide with the exception that 20 milligrams of drug were used per cubic centimeter of solution.

The initial dose of drug given by the intravenous route was 10 milligrams; for other routes doses of 20 to 40 milligrams were employed. Subsequent therapy depended on the white blood count which was obtained prior to each treatment. The dose was reduced when the white blood cells dropped below 5,000 per cubic millimeter, and therapy usually was discontinued temporarily in the presence of a leucopenia exceeding 3,000 per cubic millimeter.

Routes of therapy are listed as follows: intravenous in 16 cases, intrapleural in 3, intraperitoneal in 3, intrapericardial in 1, into peripheral tumor masses in 7, transvaginal in 16, and transabdominal in 10 cases.

In all cases an attempt was made to treat the site of disease which presented the greatest threat to the patient's welfare. The transvaginal and transabdominal approaches were used when a needle could be inserted directly into tumor masses in these areas. Only 1 site was treated at a time.

When pleural effusion or ascites occurred, a thoracentesis or paracentesis was performed and the drug was injected following the tap. One patient (Case 22) received 1 intrapericardial injection of triethylene thiophosphoramide following a pericardial tap. Intravenous therapy was reserved usually for those occasions when no tumor sites could be reached with a needle. Route of therapy varied from time to time depending on the status of the patient.

OBSERVATIONS

Results of therapy, exclusive of increased well-being and appetite, were: none in 5 cases; subjective—control of pain in 2 cases, of dyspnea in 1 case, of nausea in 1 case, of urinary frequency in 1 case; objective—regression of tumor masses in 13 cases, control of pleural effusion in 4 cases, decrease of ascites in 4 cases, control of pericardial effusion in 1 case.

TABLE II.—RESPONSE OF FAR-ADVANCED OVARIAN CARCINOMA TO PHOSPHORAMIDE THERAPY

	Survival				*Objective Improvement*			
Pathology	*No. living*	*No. lost*	*Duration, mos.*	*Average, mos.*	*No. living*	*No. lost*	*Duration, mos.*	*Average, mos.*
Serous cystadenocarcinoma	3	3	10–16 3–10	12.3 3.7	3	1	7–16 7	11.3 7
Pseudomucinous cystadenocarcinoma	2	1	5–6 3	5.5 3	2	1	5–6 1	5.5 1
Papillary adenocarcinoma	4	5	5–22 1–11	12.8 6	3	5	8–22 1–11	15.3 4.5
Undifferentiated carcinoma	0	2	0 1.5–6	0 4	0	1	0 3	0 3
Malignant dysgerminoma	1	1	13 2	13 2	1	0	13 0	13 0
Total	10	12	1–22	8	9	8	1–22	8

Table II summarizes results of therapy as related to pathologic type of disease.

SEROUS CYSTADENOCARCINOMA (CASES 1, 2, 6, 13, 17, AND 22)

Three patients are living at 16, 11, and 10 months after beginning therapy, 1 was lost to follow-up at the end of 3 months, 2 expired at 4 and 10 months respectively. Four were improved by treatment. One patient is of unusual interest.

E. B. was a 39 year old female who had complained of intermittent abdominal swelling of many months' duration. On June 10, 1954, a laparotomy was performed. The omentum which was completely involved by tumor was resected. Bilateral proliferative adherent ovarian masses were left in situ. Each of these was injected with 20 milligrams of triethylene thiophosphoramide during surgery. Two weeks postoperatively the patient developed pyelitis. A retrograde pyelogram demonstrated marked dilatation of the left ureter, minimal of the right. Chills and fever disappeared following antibiotics. Subsequently, the patient was placed on intravenously administered triethylene thiophosphoramide for 4 doses. Because suspicious nodules could be palpated in the left adnexa, therapy was continued by the transvaginal route at 1 to 3 week intervals to a total dose of 595 milligrams triethylene thiophosphoramide and 60 milligrams oxapentamethylene diethylene phosphoramide. The patient has returned to her job as a secretary and 16 months after institu-

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tion of therapy there is no palpable evidence of disease, although the primary tumors were not removed.

Although the primary sites of disease, namely bilateral ovarian tumors, were not removed, this patient has no palpable disease 16 months following resection of the omentum for extensive metastases. Dilatation of one ureter demonstrated postoperatively suggested constriction by tumor and further indicated the extensive nature of this patient's disease.

PSEUDOMUCINOUS CYSTADENOCARCINOMA (CASES 3, 5, AND 16)

Two patients are alive and improved, 6 and 5 months after institution of therapy. The third had temporary improvement in nausea, vomiting, azotemia, and ascites but died from massive abdominal disease less than 3 months after beginning treatment.

L. D., a 41 year old school teacher and mother of 2 small children, had an exploratory laparotomy in March 1954, at which time a 12 by 15 centimeter left ovarian mass, many 2 by 4 centimeter metastases to omentum, mesentery, liver, small and large bowel, and numerous 1 centimeter peritoneal nodes were found. Biopsy of the omentum revealed pseudomucinous cystadenocarcinoma. The patient was started on transabdominal injections of triethylene thiophosphoramide postoperativeiy and had received 385 milligrams of triethylene thiophosphoramide and 40 milligrams of oxapentamethylene diethylene phosphoramide by September 1955. She is continuing to teach full time and keep house, 6 months after institution of therapy, although there has been only partial regression of palpable abdominal nodules.

This patient had widespread abdominal metastases at surgery and only adequate tissue for biopsy was removed. The patient has been able to continue teaching and housework while on maintenance therapy with phosphoramides. Although her disease has shown only minimal regression it is apparently controlled.

PAPILLARY ADENOCARCINOMA (CASES 4, 7, 8, 9, 12, 14, 15, 19, AND 21)

This group comprised the largest in the series. Four patients are alive 5 to 22 months after beginning treatment. One continues to re-form ascitic fluid at almost the same rate as when first seen, 3 are improved. Four expired 1, 3, 10, and 10 months and 1 was lost to follow-up 11 months after institution of therapy.

M. P., a 71 year old white female, had her first laparotomy for a papillary adenocarcinoma of the ovary in December 1952. At a second operation in April 1953 there was generalized seeding of the pelvic peritoneum, angulation of ureters, and infiltration of the base of the bladder. Twelve radon seeds were implanted via the vagina. Progressive signs and symptoms of intestinal obstruction developed and emergency colostomy was required in December 1953. At this time the patient was suffering from distressing urinary frequency and a nodular pelvic mass was palpable. Postoperatively the patient received a course of intravenously administered triethylene thiophosphoramide. Subsequently, transvaginal administration was substituted and urinary frequency diminished markedly in 6 weeks. The pelvic mass disappeared by May 1954 and the colostomy was closed. The patient has received injections of triethylene thiophosphoramide administered every 2 to 4 weeks since that time. Her total dose of drug has been 520 milligrams of triethylene thiophosphoramide and 30 milligrams of oxapentamethylene diethylene phosphoramide. She takes cross country bus trips, cares for an invalid sister, and is still leading a very active life 22 months after institution of therapy. There is no palpable disease at this time.

Transvaginal injections of triethylene thiophosphoramide were associated with regression of a pelvic tumor. There has been no recurrence of obstructive symptoms since closure of the patient's colostomy.

UNDIFFERENTIATED OVARIAN CARCINOMA (CASES 11 AND 18)

The 2 patients in this group expired in 1.5 and 4 months respectively after institution of therapy. The first died from complications of the disease, the second from a cerebral thrombosis.

B. D., a 62 year old white female, had a panhysterectomy and bilateral salpingo-oophorectomy in October 1953 at which time the carcinomatous area in a large ovarian cyst was found to be intimately adherent to the lateral pelvic wall and all posterior structures. Postoperative irradiation was administered. In April 1954, a large pelvic mass was palpable. Transvaginal injections of triethylene thiophosphoramide were administered at 1 to 4 week intervals with a total dose of

only 215 milligrams in 5 months. There was temporary regression of the mass and the patient returned to work. In September 1954 a series of cerebrovascular accidents developed. The patient expired 1 month later. Postmortem examination revealed widespread tumor throughout the abdomen, and areas of infarction in the kidneys and brain.

The multiple thrombotic phenomena in this case were considered to be a complication of ovarian carcinoma. In retrospect, it was thought that the amount of triethylene thiophosphoramide given to this patient was too little and doses were too far spaced for maximum effectiveness.

MALIGNANT DYSGERMINOMA (CASES 10 AND 20)

Of the 2 patients in this group, 1 (Case 20) had massive rapidly progressive disease, terminating in intestinal obstruction and showing no improvement with therapy; the second demonstrated a different response.

P. C., a 35 year old female, had a left salpingo-oophorectomy with a pathologic diagnosis of malignant dysgerminoma in October 1953, a hysterectomy and right salpingo-oophorectomy in December 1953, and was found on laparotomy in August 1954 to have many tumor masses in the omentum and mesentery, a 2 centimeter mass in the small bowel which was resected, and a large fixed pelvic mass which was left in place. Injections of triethylene thiophosphoramide were given by the transvaginal route at 1 to 2 week intervals to a total dose of 780 milligrams from September 1, 1954 to August 30, 1955. Oxapentamethylene diethylene phosphoramide was substituted during a shortage of the other phosphoramide. The patient has continued a very active life during the 13 months of therapy. There has been no palpable evidence of disease for 10 months. The patient is moderately anemic, probably due to prolonged chemotherapy.

This patient has shown a good response to chemotherapy. Discontinuation of the drug was considered but rejected on the basis that chemotherapy has not been curative in our hands and residual disease was therefore assumed to be present.

COMMENTS

Although this series of cases is small, all patients included had evidence of widespread ovarian carcinoma. Death usually occurs within 2 years in such patients when operation has been incomplete. Ten of the patients treated with triethylene thiophosphoramide are alive 5 to 22 months following the institution of chemotherapy. Two were lost to follow-up.

Of the 10 who have expired, 7 patients had some degree of palliation for periods of from 1 to 7 months.

Triethylene thiophosphoramide is not difficult to administer even when given transvaginally or transabdominally. Treatment is easily given in the clinic or the office, and because there are minimal clinical side effects it is compatible with continuation of normal activities. Reasonable care is needed to avoid infection at the site of injection.

In the presence of extensive disease, treatment must be maintained at hematopoietic tolerance. Prophylactic antibiotic medication is not recommended in order to avoid the hazards of side effects and development of drug resistant infection. However, when infection occurs it should be treated promptly and adequately. Prolonged therapy with the phosphoramides appears to be associated with varying degrees of anemia in many cases. It is much more apt to occur with oxapentamethylene diethylene phosphoramide injections and may be severe following this drug. Since anemia is frequently associated with far advanced cancer and since anemia does not always occur with phosphoramide therapy, it is assumed that other factors may be involved.

SUMMARY AND CONCLUSIONS

1. Observations on the treatment of far advanced ovarian carcinoma with phosphoramide drugs are reported.

2. Twenty-two patients were treated for periods of 1 to 22 months with total doses of 110 to 780 milligrams (average 353 milligrams) of N-N′-N″ triethylene thiophosphoramide. Short periods of substitution therapy with N-3 (oxapentamethylene) N-N′-diethylene phosphoramide were used in 8 cases.

3. Routes of therapy include intravenous, intrapleural, intraperitoneal, intrapericar-

dial, intratumor, transvaginal, and transabdominal. In 2 cases abdominal masses were injected during laparotomy.

4. Objective improvement included regression of tumor masses and control of pleural, pericardial, and peritoneal effusion.

5. Ten patients are alive 1 to 22 months following institution of therapy; of 12 who died or were lost to follow-up, 8 showed improvement for periods ranging from 1 to 11 months.

6. Therapy with phosphoramide drugs appears to be palliative only and must be continued in order to achieve and maintain control of disease.

7. The observations herein reported appear to warrant further therapeutic trials with triethylene thiophosphoramide in ovarian carcinoma.

REFERENCES

1. Ackerman, L. V., and del Regato, J. A. Cancer: Diagnosis, Treatment and Prognosis. Pp. 836, 865. St. Louis: C. V. Mosby Co., 1954.
2. Griboff, S. I. The rationale and clinical use of steroid hormones in cancer. Arch. Int. M., 1952, 89: 812.
3. Kottmeier. Discussion of Wetterdal, P. Some aspects of the diagnosis and treatment of carcinoma of the ovary. Acta obst. gyn. scand., 1949, 28: 510.

THE BILIARY EXCRETION OF ERYTHROMYCIN (ILOTYCIN)

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THE PURPOSE OF THIS INVESTIGATION was to determine whether erythromycin (ilotycin or erythrocin) was effective against types of pathogens found in the biliary tract and whether, after its oral administration, erythromycin was excreted in the bile in sufficient concentration to have an inhibitory effect upon these bacteria. The preparation used in this study was ilotycin. Our interest in this subject was promoted by the successful clinical use of this agent in certain patients with gram-negative bacterial infections which had been resistant to therapy with other broad spectrum antibiotics.

Welch has classified erythromycin as a member of the broad spectrum group of antibiotics (which includes tetracycline, chlortetracycline, oxytetracycline, and chloramphenicol), because it is effective against bacteria, viruses, and rickettsiae. In vitro it has a penicillin-like effect on gram-positive bacteria; in high concentrations, it exerts a bacteriostatic effect upon gram-negative bacteria as well.

Erythromycin has been found to be excreted in the bile after its oral administration, by Heilman, Herrell, Wellman, and Geraci. This antibacterial agent was also found by Pulaski and Fusillo to be excreted into the gallbladder with a patent cystic duct following its oral administration. These authors have recorded the concentrations of erythromycin and other antibiotics in the blood serum and gallbladder bile.

The limited use of erythromycin in the treatment of gram-negative infections so far reported may be due in part to the fact that sensitivity tests by the universally used paper disc method described by Kolmer and associates show most gram-negative bacteria to be resistant. Our own paper disc tests have substantiated this observation as we found erythromycin to be only slightly effective against 21 strains of Escherichia coli and ineffective against 18 other strains. Similar disappointing results were obtained with various strains of Salmonella typhosa.

These unfavorable findings with the paper disc method may be due to the low concentrations of erythromycin (10 gamma per disc) with which the discs are impregnated. A preferable procedure, in our opinion, for testing this agent is the test tube dilution method by which it is possible to place the test micro-organism in intimate contact with a much higher antibiotic concentration. In addition, the test tube dilution method may be modified to approximate more closely conditions in the biliary tract by testing in the presence of a high concentration (50 per cent by volume) of liver bile.

THE PRESENT INVESTIGATION

Bacteriostatic studies. In this investigation a series of pathogens of the type found in the biliary tract were tested for the inhibitory or bacteriostatic level of erythromycin by the test tube dilution method (3). The procedure was as follows:

In a series of test tubes was placed 0.5 milliliter of graded dilutions of erythromycin. To each was added 1 milliliter of clear sterile liver bile (50 per cent of the total volume) and 0.5 milliliter of quadruple strength inoculated nutrient broth. After incubation at 37 degrees for 24 hours, all tubes were examined for evidence of growth. The end point was the highest dilution of the antibiotic showing no visible evidence of growth. The results are shown in Table I.

The authors are indebted for part of the clinical material used in these tests to surgical associates of the New York, Roosevelt, University and Bellevue Hospitals.

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TABLE I.—RESULTS OF TEST TUBE DILUTION BACTERIOSTATIC TESTS OF ERYTHROMYCIN WITH VARIOUS PATHOGENS OF THE BILIARY TRACT, WITH AND WITHOUT THE PRESENCE OF LIVER BILE

Organism	*Minimum inhibitory concentration (mcgm./ml.)*	
	With 50 per cent bile	*No bile*
Micrococcus pyogenes (Staphylococcus aureus)	0.25	0.13
Streptococcus, beta	0.38	0.18
Streptococcus, alpha	1.5	0.38
Escherichia coli	250.0	90.0
Salmonella typhosa	190.0	75.0

TABLE II.—CONCENTRATION OF ERYTHROMYCIN IN GALLBLADDER BILE AND BLOOD FOLLOWING MULTIPLE DOSES BY MOUTH

Patient No.	*Dosage, mgm.*	*Concentration (mcgm./ml.) Hours after last dose*							
		Bile				*Blood*			
		1	2	3	4	1	2	3	4
1	200		80.						
2	400		35.				0.4		
3	400		80.				0.4		
4	400	96.					3.0		
5	400		250.				1.0		

To determine whether this inhibitory action was bactericidal as well as bacteriostatic, those culture tubes remaining clear were subcultured into 10 milliliters of nutrient broth, without bile, and reincubated. Since all subcultures up to 1,000 gammas per milliliter (the highest concentration set up) became positive, the suppression of growth was interpreted as bacteriostatic.

These procedures were carried out to simulate, as far as possible, conditions in the biliary tract. For comparative purposes all test tube sensitivity tests were run in parallel, with and without the presence of bile. The results of both series of tests are shown in Table I. It is here seen that the concentrations of erythromycin necessary for inhibitory action was considerably greater in the presence of bile.

EXCRETION STUDIES

Gallbladder. In 6 patients having cholecystectomy, erythromycin was given in dosages of 200 milligrams or 400 milligrams 4 times the day preceding operation and once—1 or 2 hours before laparotomy. For the 5 patients having patent cystic ducts, the concentrations of erythromycin in the gallbladder bile obtained at operations and the corresponding blood serum concentrations are shown in Table II. In 1 patient having an occluded cystic duct with stones but no bile in the gallbladder, the specimen of bile obtained from the common duct showed a concentration of 8 micrograms per milliliter.

Table II shows that inhibitory concentrations of erythromycin in bile were obtained in each patient for all the pathogens studied except Escherichia coli and Salmonella typhosa. In 1 patient, however (No. 5), a high bacteriostatic concentration was obtained, sufficient to inhibit both Escherichia coli and Salmonella typhosa.

Liver bile. The concentration of erythromycin in liver bile was determined by obtaining bile specimens by T-tube drainage

TABLE III.—CONCENTRATION OF ERYTHROMYCIN IN BILE OBTAINED BY T-TUBE DRAINAGE IN POSTCHOLECYSTECTOMY PATIENTS

Patient	*Days postop.*	*Dosage, mgm.*	*Concentration (mcgm./ml.) Hours after last dose*								
			Bile					*Blood*			
			1	2	3	4	5	1	2	3	4
A.K.	14	200		5.		6.			.5		.5
E.A.	76	200		40.		45.					
A.Z.	7	200		15.		10.			1.5		1.0
M.S.	10	200		25.		30.					
M.B.	17	200		32.							
L.B.	11	400		90.		110.					
M.S.	4	400		35.		35.			4.		4.5
M.M.	8	400		26.5		26.5			12.		18.
E.W.	4	400		22.		27.			7.		9.
E.T.	7	400		15.					0.5		
M.A.		400		10.					2.		2.
M.O.	5	500	475.		260.		225.	8.5		1.	
C.T.	6	500	800.		380.		320.	16.		12.	

of the common duct, in postcholecystectomy patients. Each was given erythromycin by mouth 4 times during the day preceding the test and once in the morning of the test. The dosage varied from 200 to 500 milligrams, as shown in Table III.

It is seen in Table III that all patients receiving dosages of 200 or 400 milligrams had a concentration of erythromycin inhibitory for all pathogens tested, except Escherichia coli and Salmonella typhosa. In the patients receiving dosages of 500 milligrams of erythromycin, bile concentrations were obtained sufficient to inhibit both Escherichia coli and Salmonella typhosa.

Of those patients receiving dosages of 500 milligrams, the actual bacteriostatic levels for the patients' own bacteria were for patient M. O. 240 micrograms per milliliter, and for patient C. T. 250 micrograms per milliliter. These concentrations were exceeded in both the specimens of bile.

Duodenal bile. In order to determine the concentration of erythromycin obtainable in duodenal bile, 2 additional patients were studied who by roentgenographic studies had functioning gallbladders containing stones. The day preceding duodenal drainage each patient was given 4 doses of erythromycin, 1 in dosage of 200 milligrams and the other 400 milligrams. Preceding the passage of the duodenal tube, a similar dose of erythromycin was given to each patient. Following the passage of the duodenal tube, specimens of bile and blood were obtained at the same time intervals as for the T-tube drainage patients.

In the patient having 5 doses of 200 milligrams of erythromycin, the duodenal bile showed at 2 and 4 hours 10 micrograms per milliliter and 15 micrograms per milliliter, respectively, while blood taken at the same time gave concentrations of 8 micrograms per milliliter and 6 micrograms per milliliter. In the other patient, dosages of 400 milligrams of erythromycin gave at 3 and 5 hours concentrations in the duodenal bile of 110 micrograms per milliliter and 105 micrograms per milliliter.

Clinical use. Erythromycin is being used at the present time in patients with chronic cholecystitis and in chronic cholangitis following cholecystectomy. The results of this investigation will be the basis of a subsequent report.

SUMMARY AND CONCLUSIONS

1. The concentrations of erythromycin necessary to have an inhibitory or bacteriostatic effect upon a series of pathogens of the biliary tract have been determined by the test tube dilution method, with and without the presence of bile.

2. For erythromycin the test tube dilution method is considered preferable to the paper disc method.

3. Following multiple oral doses of 200 or 400 milligrams of erythromycin, gallbladder bile obtained at the time of cholecystectomy gave concentrations inhibitory for pathogens other than Escherichia coli and Salmonella typhosa. A concentration of erythromycin sufficient to inhibit both Escherichia coli and Salmonella typhosa was obtained in 1 patient having a dosage of 400 milligrams.

4. In postcholecystectomy patients having multiple oral dosage of 200 and 400 milligrams of erythromycin, concentrations of erythromycin were found in the T-tube drainage bile inhibitory for the pathogens tested other than Escherichia coli and Salmonella typhosa. Concentrations inhibitory for these organisms were obtained after increasing the dosage to 500 milligrams.

REFERENCES

1. HEILMAN, F. R., HERRELL, W. E., WELLMAN, W. E., and GERACI, J. E. Some laboratory and clinical observations on a new antibiotic, erythromycin (ilotycin). Proc. Mayo Clin., 1952, 27: 285.
2. KOLMER, J. A., SPALDING, E., and ROBINSON, H. W. Approved Laboratory Technique. 5th ed., p. 557. New York: Appleton-Century-Crofts, Inc., 1951.
3. Method of Assay and Certification of Antibiotics and Antibiotic-Containing Drugs. Part 141A, Dept. of Health, Education and Welfare. Food and Drug Administration. Washington, D. C., March 1, 1954.
4. PULASKI, E. J., and FUSILLO, M. H. Gallbladder bile concentrations of the major antibiotics following intravenous administration. Surg. Gyn. Obst., 1955, 100: 571.
5. WELCH, H. Antibiotic Therapy. P. 169. New York: Medical Encyclopedia, Inc.

VAGOTOMY AND PYLORECTOMY IN THE TREATMENT OF DUODENAL ULCERATION

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IN CONSIDERING the problem of peptic ulceration, two facts emerge, namely that the cause is unknown and that control of established ulceration depends upon the elimination of free hydrochloric acid from the upper alimentary canal. In the surgical treatment of ulceration, attempts at achieving the latter object have been met by utilizing three principles, namely diversion of the gastric contents as in gastroenterostomy, ablation of the oxyntic cell bearing mucosa of the stomach as in subtotal gastrectomy, and interruption of the pathways of stimulation of acid secretion by vagotomy and combined procedures. The acceptability of these procedures is measured not only by their effectiveness in curing the original ulcer and preventing recurrence but also by the extent to which they are accompanied by undesirable postoperative sequelae.

Subtotal gastrectomy has proved so effective in attaining cure of peptic ulcer that it has come to be regarded as a yardstick against which all other operative procedures are measured. However, its very success in one direction has tended to throw into relief the incidence of untoward conditions following the operation and so the search goes on for the Utopian treatment.

The subtotal resection, by directing attack against the site of acid secretion by removing the major part of the stomach, has the disadvantage of depriving the subject of other valuable properties of that viscus among which is its reservoir capacity. Much is known of the part played by the stomach in the nutritional economy of the patient, but nutritional defects can and do occur after subtotal gastrectomy, e.g., failure to put on weight, anemia and vitamin deficiencies, and with the possibility of more subtle functions of the stomach that may yet remain to be discovered, we should not assume that it is as surgically expendable as perhaps we have done too readily in the past.

In order to obtain maximum reduction of acid secretion at the same time as retaining the greatest amount of stomach, interruption of the stimulatory pathways offers itself as a compromise worthy of consideration. Stimulation of acid secretion has a dual mechanism, neurogenic via the vagi, and humoral, consequent upon the production of gastrin by the mucosa of the pyloric antrum.

Section of the vagi and removal of the pyloric antrum then is a combination that should leave the oxyntic cell functionally isolated. Both of these procedures when carried out alone in the past have been proved failures as treatment of peptic ulceration. Vagotomy by itself is attended by troublesome gastric stasis and pyloric antrectomy, synonymous with the low partial gastrectomies before the subtotal era, has a too high risk of recurrent ulceration. In combination one acts in support of the other. Pylorectomy overcomes the gastric stasis of vagotomy and the latter by eliminating neurogenic secretion enhances the effect of depriving the oxyntic cells of humoral control. The operation of vagotomy with limited gastrectomy has been developed and advocated strongly by Johnson in 1950 and 1951 and by Johnson and Orr in 1953 and 1954 although in the latter papers the authors ad-

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vocate a two-third gastrectomy in combination with vagotomy. Wells in 1955 also advocates vagotomy with hemigastrectomy as the treatment of choice in duodenal ulceration.

Since January 1952 vagotomy with pylorectomy (one-third gastrectomy) has been the standard operative treatment for duodenal ulcer in this unit and up to the end of 1954, 198 patients had been operated upon.

It is pertinent at this stage to discuss more specifically the problem of management of peptic ulcer as it confronts us in Hong Kong. The majority of reports that appear on this topic concern patient series in the Occident. We believe, therefore, that this commentary will be of interest, concerned, as it is, with peptic ulcer occurring in Chinese and a survey of patients who have undergone vagotomy and pylorectomy for duodenal ulcer.

PEPTIC ULCER IN HONG KONG

Peptic ulceration is a common disease in Hong Kong among the local Chinese population. Admissions to the Surgical Professorial Unit for the condition constituted 5 per cent of the total admissions during 1954. In our patients men and women were affected in the ratio of 5 to 1 in the case of duodenal ulcer and 3 to 1 in the case of gastric ulcer. There does not appear to be any particular somatotype association, and we have encountered patients of widely varying habitat, domicile, trade, and income groups.

The finding by Aird that subjects of blood group O have a 35 per cent greater liability to develop peptic ulcer than those in other blood groups of the United Kingdom population prompted us to look for a similar correlation among our patients. Although on a small scale, the significance of investigating this point in 120 patients is accentuated by the different distribution of blood groups in the normal populace of the East compared to that in the West. As reference to Table I shows, peptic ulcer was much more commonly encountered in subjects with group O blood to the extent of a 40 per cent greater incidence in excess of its occurrence in individuals of the other groups.

TABLE I.—INCIDENCE OF PEPTIC ULCER RELATED TO PATIENTS' BLOOD GROUP AND COMPARED WITH A CONTROL DISTRIBUTION OF BLOOD GROUPS AMONG THE POPULATION OF HONG KONG

Group	*Control*	*Disease*	*Per cent increase or decrease on control*
	ENGLAND (AIRD 1954)		
O.....	47	55.4	+17.9
A.....	40.99	34.67	—15.4
B.....	8.98	7.44	—17.1
AB.....	3.03	2.49	—17.9
	HONG KONG		
O.....	43	54	+25
A.....	24	20	—16
B.....	28	22	—21
AB.....	5	4	—20

Treatment is dictated to a large measure by conditions prevailing in the colony. Due to the influx of refugees, overpopulation exists and living conditions and means of making a livelihood are rigorous for many of the public ward class of patient. Because of this fact, effective medical treatment of peptic ulcer is a luxury impossible to obtain by the general population. Hospital bed space cannot be reserved for the length of time necessary to stabilize an ulcer patient who in any case would find the regime too exacting for continuance on return home. Many of these patients live in the confined space of a cubicle shared with other families in tenement buildings or on a fishing junk or sampan. Food is often prepared under equally difficult conditions or bought ready cooked from itinerant street vendors. To emphasize further the drawbacks confronting medical treatment is the fact that to Chinese, dairy products, which are the mainstay of a bland ulcer diet, are unpalatable and of equal importance is that they are expensive in the colony. To such individuals speedy relief from a life of semi-invalidism imposed by peptic ulceration and a return to full working capacity is a real necessity. This is not to say that surgery is offered as the only mode of treatment to all patients who present. For the patient with early symptoms and an uncomplicated his-

tory a trial of out-patient medical treatment is prescribed. However, it is our experience that the majority of patients delay reporting until complications ensue, as Table II reveals, and it is for these cases that we believe it encumbent to advise surgical intervention without delay as well as for those who do not show a satisfactory early response to conservative measures.

As an outcome of this philosophy, patients who are admitted to the unit with ulcer perforation are treated by operative closure and then subjected to definitive surgery during the same period of hospitalization. Vagotomy with pylorectomy is usually carried out in these cases 2 to 3 weeks after closure of the perforation within which time the patient's general condition has sufficiently improved. Turner, in reviewing a series of 244 cases of perforated peptic ulcer treated at the Presbyterian Hospital, New York, during a 20 year period, observed that 85.3 per cent of the patients experienced ulcer symptoms following simple closure of the perforation and 38.5 per cent who subsequently recovered had further surgical treatment. In his view, these figures served to show the fallacy of the one time prevalent impression, that peptic ulcers commonly heal and become asymptomatic following perforation, and he suggested that prophylactic surgery be strongly considered in the immediate postoperative period of these patients. This aspect of the subject is being considered in a separate paper.

The predominant variety of duodenal ulcer occurring in Hong Kong is the penetrating type and Table II shows that complications due to penetration of an ulcer, i.e., bleeding and perforation, are very much more common than those produced by cicatrization.

In subjecting vagotomy and pylorectomy to an extended trial, it was hoped to find in this combination a means of curing duodenal ulcer at the same time as avoiding nutritional defects by retaining as much as possible of the reservoir property of the stomach by leaving a large gastric remnant. It was believed that these two objectives were of special importance to the local patients. Chinese eat two main meals a day each consisting of rice, some cooked vegetable, and a little meat or fish. Rice is the mainstay of the meal. It is nutritious, hunger satisfying, but has to be taken in quantity. Once in the alimentary canal it absorbs water and increases its bulk to which the normal stomach accommodates readily enough when it is accustomed to doing so. Chinese have observed that, on returning to the East after a protracted stay in other countries and after eating Western food, they have found themselves unable to take as much rice, for a time, as they previously had. This seems to indicate that on the average the Chinese diet is rather more bulky than that in Western countries making conservation of space in the upper alimentary canal a matter for some consideration in peptic ulcer surgery in this area.

When considering nutritional defects which may occur after operation, it has to be appreciated that a proportion of these patients are on the borderline of nutritional inadequacy because of economic circumstances, and it is as well to recall that the early work on vitamin deficiency states was carried out in Southeast Asia on beri-beri. To this day, polished rice is still eaten by Asiatics and vitamin B deficiency remains a potential threat at all times. Any added strain on the subjects' nutritional reserves is liable to expose a deficiency state and may be illustrated by the thiamine deficiency that patients with thyrotoxicosis in this area quite commonly exhibit. Welbourn, Hughes, and Wells have shown that hypovitaminosis B is not uncommon following subtotal gastrectomy in European patients even with their appreciably higher standard of living.

During the 3 year period 1952 to 1954, 244 patients were operated upon for peptic ulcer in this unit. Operations for duodenal ulcer were predominant in the ratio of 8 to 1. Table III illustrates the distribution of the various operative procedures used. In the main, the subtotal gastrectomy patients are

those operated upon before the procedure of vagotomy and pylorectomy was adopted as our standad technique, variations of which concern the type of gastrojejunal anastomosis and the manner of duodenal closure dictated by the conditions present at the operation. All things being equal we choose to carry out a perabdominal transhiatal vagotomy and a one-third resection of the stomach with a short loop retrocolic gastrojejunal anastomosis. In those patients in whom a duodenal ulcer is found to be grossly penetrating the head of the pancreas we resort to a Bancroft procedure to remove the pyloric mucosa or a two staged procedure, leaving the pyloric antrum for excision after an interval allowed for healing, rather than embarking on a potentially hazardous dissection beyond the ulcer. Antecolic anastomoses have been necessitated uncommonly because of shortness of the transverse mesocolon denying space for a retrocolic union. When a Hofmeister valve has been incorporated in the anastomosis it has been done more to reduce the gastrojejunal stoma to a reasonable size rather than in the belief that it has any influence on afferent loop reflux.

Vagotomy and pylorectomy have been used in a few cases of gastric ulcer situated low down on the lesser curvature where their benign nature has not been in doubt and when one-third gastrectomy has been adequate for their removal. Ulcers situated higher up in the stomach have been dealt with by subtotal gastrectomy.

TABLE II.—INCIDENCE OF COMPLICATIONS IN 200 PATIENTS SUFFERING FROM DUODENAL ULCER

Complications	*No. of patients*	*Per cent*
Melena or hematemesis	50	25
Perforation	55	27.5
Pyloric stenosis	18	9
Hemorrhage and perforation	9	4.5
Hemorrhage and stenosis	23	11.5
Perforation and stenosis	3	1.5
Hemorrhage, perforation, and stenosis	1	0.5
No complications	41	20.5
	200	100

i.e., 41.5 per cent of ulcers associated with hemorrhage, 34 per cent perforated, and 22.5 per cent became stenotic.

Hemorrhage was not considered a complication unless it was sufficiently severe to be obvious to the patient. The finding of occult blood in the stool alone was not included.

The criterion for stenosis was the presence of obvious symptoms of gastric retention or a significant residue in the stomach at 5 hours after a barium meal.

THE OPERATION

In the preoperative preparation of the patient, attention is paid to the correction of fluid and electrolyte depletion and a minimum hemoglobin level of 10 grams is ensured by blood transfusion when necessary. To ensure adequate reserves of the water soluble vitamins, ascorbic acid and the vitamin B complex are administered routinely from the time of hospital admission through the immediate postoperative convalescent period.

Anesthesia is induced with pentothal and maintained with pentothal, gas, and oxygen, relaxation being obtained by the use of curidium or another relaxant.

A midline epigastric incision usually gives adequate access to the extremes of the operation field for the vagus resection and the duodenal closure, but if restricted it may be carried up to the subcostal margin to the left of the ensiform process. Very occasionally it is found helpful to divide the ligamentum teres of the liver when this structure interferes with exposure. Having opened the abdomen and confirmed the presence of an ulcer, the remainder of the peritoneal cavity is surveyed for concomitant pathologic conditions. Vagotomy is the first step in the operation. The stomach is drawn down by the application of tissue forceps and the abdominal portion of the esophagus put on a gentle stretch. We do not find it necessary to mobilize the left lobe of the liver by dividing the triangular ligament to gain access to the vagi and a deep retractor to draw the lobe aside is all that is required. The peritoneum over the anterior aspect of the esophagus is incised and the esophagus mobilized digitally to enable a length of narrow rubber tubing to be placed around it for traction purposes. This device is useful to bring down the esophagus and place the vagi on the stretch, enabling them to be recognized by palpation as taut cord-like structures. The left vagus can usually be seen lying on the front of the esophagus but the right, lying posteriorly, is best identified and hooked forward with the fin-

ger until it is possible to grasp it in long forceps. Although most often applied closely to the esophageal wall and reasonably constant in position the main vagal trunks may be situated at a little distance from the esophagus on the medial side in which case they are not so readily identified and they may not be included in the rubber sling. In these circumstances folds of peritoneum are easily mistaken for the nerves. The vagi are divided between clamps and the ends ligated as also are any smaller branches which may be identified in the same manner as the parent trunks. It is usually possible to perform this stage of the operation without any bleeding of consequence but occasionally it is necessary to ligate or coagulate small vessels on the anterior aspect of the esophagus that have been divided during the peritoneal incision. The vagotomy completed, an abdominal pack is placed into the area, the rubber sling left in situ, and attention next directed to the stomach.

In carrying out the gastrectomy stage of the operation our object is to leave as much stomach as is consistent with removing that portion responsible for the production of gastrin. This latter function is an attribute of the pyloric antrum which by anatomic definition lies between the incisura angularis and the pyloric sphincter. However, it is not the anatomic, so much as the physiologic antrum with which we are concerned, the limits of which cannot, of course, be defined by naked eye inspection. Furthermore, as the incisura is essentially a radiologic landmark there is no accurate criterion for delimiting the pyloric antrum at operation. Accordingly we elect to excise the distal third of the stomach and believe that by so doing we are achieving our purpose. Limited gastrectomy is proceeded with in the accepted manner. The left gastric vessels are divided on the lesser curvature, and we endeavor to conserve the gastroepiploic arch. The duodenum is mobilized, divided, and closed whenever possible but the Bancroft maneuver or two stage procedure is utilized on occasions when stump closure is liable to prove precarious. Continuity of the alimentary canal is usually restored by drawing up the most proximal loop of jejunum through an opening made in the avascular area of the transverse mesocolon to the left of the middle colic vessels and a Polya or Hofmeister valved gastrojejunal anastomosis effected. The afferent loop is made as short as possible without kinking, usually about 4 inches, and is applied to the lesser curvature of the stomach. On completing the anastomosis the gastric remnant is drawn down below the level of the transverse mesocolon and fixed to the cut edge of the mesocolic window with a few interrupted sutures. In several respects this one-third gastric resection is easier to carry out than a subtotal removal of the stomach; the left gastric vessels are divided at a level that is in easy reach and the anastomosis can invariably be performed outside the abdomen.

The operation is completed by checking the vagotomy site for hemostasis, and here again the rubber sling previously left in place is a useful aid to the inspection. The peritoneum over the esophagus is not sutured, and we have seen no evidence of postoperative diaphragmatic hiatus herniation. The abdomen is closed without drainage unless there is any doubt about the security of the duodenal closure.

Postoperatively, parenteral fluids and electrolytes are continued for 48 hours with intermittent gastric aspiration. Small amounts of water are allowed on the first day and the oral intake progressively increased as intestinal motility returns. Congee, which is a thin rice gruel, is served by the fifth day and a normal rice diet restored at the end of a week. Penicillin and streptomycin are given after operation until the patient is apyrexial. In this connection it is of interest to note that an exacerbation of latent malaria is not infrequently found to be the cause of a postoperative pyrexia when more common causes have been eliminated. In such instances, the temperature chart is not often of the intermittent configuration that typifies malaria but the pyrexia is sus-

tained and continuous. Bearing the possibility in mind and recognizing the parasites in the blood smear enable effective treatment to be instituted without delay. Disturbing the spleen by manipulating the stomach at operation is the probable trigger mechanism of these malarial relapses.

Before discharging the patient from the hospital, usually about the tenth to twelfth postoperative day, a further fractional test meal study is made for comparison with the preoperative record. In the majority of patients, in whom such a comparison was made, complete elimination of free acid from the meal was disclosed. However, satisfactory reduction of acidity was not obtained in all patients, some still manifested varying levels of free acid in their comparison test meal. These failures are most likely explained by incomplete vagal denervation of the gastric remnant or insufficient removal of pyloric mucosa. While division of the main vagal trunks is accomplished readily enough at operation it appears that small branches may evade detection to an extent that enables neurogenic acid secretion to continue unchecked. Another possibility incriminates the secretory cells themselves in which a high innate level of secretion may be uninfluenced by the removal of stimulatory pathways. Should this be the case, then subtotal gastrectomy would be obligatory for producing achlorhydria in such patients.

So far we have regarded these test meal studies more from the academic interest viewpoint rather than as an indication for subjecting the patient to further surgery when reduction of acid has not been demonstrated. This policy, however, may have to be revised if any of these patients subsequently develops stomal ulceration, and none has yet done so to our knowledge. One patient subjected to vagotomy and first stage gastrectomy showed persistent free acid after his first operation. He failed to attend for the second stage until he developed a stomal ulcer and then was submitted to a second stage pylorectomy. After this procedure his pain disappeared but free acid still persisted. It is too early yet to say whether he will require a subtotal gastrectomy though this seems probable.

TABLE III.—OPERATIVE PROCEDURES FOR PEPTIC ULCER IN 244 CASES

	Duodenal ulcer	*Gastric ulcer*	
VAGOTOMY AND PYLORECTOMY			
Retrocolic Hofmeister			
With Bancroft	4		
Without Bancroft	95	2	
2 stage operation	1		
Retrocolic Polya			
With Bancroft	18		
Without Bancroft	40		
2 stage operation	5		
Antecolic Hofmeister			
Without Bancroft	4		
Antecolic Polya			
With Bancroft	1		
Without Bancroft	3		
Billroth I anastomosis	18	2	
Total	189	4	193
SUBTOTAL GASTRECTOMY			
Retrocolic Hofmeister			
With Bancroft	1	8	
Retrocolic Polya			
With Bancroft	3		
Without Bancroft	21	7	
2 stage operation	2		
Antecolic Hofmeister			
Without Bancroft	1		
Antecolic Polya			
Without Bancroft		4	
Billroth I anastomosis		4	
Total	28	23	51

RESULTS OF OPERATION

On their return home after operation the patients are seen for review of their immediate convalescent progress at an outpatient clinic located in the midst of a densely populated area in the town. Owing to the pressure of routine work at this clinic, it has not been possible to provide regular long term follow-up facilities, as we would like, and such as is possible in most centers in Great Britain. However, we felt it desirable to review the results in the ulcer patients with particular reference to the vagotomy and pylorectomy series to determine whether or not our declared expectations of the operation had been realized and to decide if the policy was worthy of continuance. Accordingly, a special clinic was organized in the main hospital building and patients were requested to attend by letter for prearranged appointments.

TABLE IV.—FOLLOW-UP OF 118 PATIENTS

Operation	*No. of patients*	*Grading* *A*	*B*	*C*	*D*
DUODENAL ULCER					
Subtotal gastrectomy					
Antecolic	9	7	2	0	0
Retrocolic	1	0	1	0	0
Vagotomy and pylorectomy					
Antecolic	3	3	0	0	0
Retrocolic	86	64	17	1	4
Billroth	3	3	0	0	0
Pylorectomy alone	1	1	0	0	0
Total	103	78	20	1	4
GASTRIC ULCER AND COMBINED GASTRIC AND DUODENAL ULCER					
Subtotal gastrectomy					
Antecolic	2	1	0	0	1
Retrocolic	6	6	0	0	0
Billroth	2	1	0	1	0
Vagotomy and pylorectomy					
Retrocolic	5	3	0	1	1
Total	15	11	0	2	2

All patients operated upon for peptic ulcer during the period from 1950 to the end of 1954 were circularized. Of these, 118 or 48.3 per cent attended for follow-up which was conducted along the lines of a personal interview and questionary and a clinical examination. Of 189 patients who had had vagotomy and pylorectomy for duodenal ulcer 92 or 48.6 per cent attended.

While the incompleteness of the attendance is a shortcoming of the follow-up and makes conclusions therefrom tentative rather than conclusive, nevertheless, it is a limitation that we have had to accept. Local conditions that contribute to the difficulty of maintaining contact with patients are: frequent population movements, patients living in remote parts of the colony, disinclination to take time off work of those employed casually, and inaccuracies introduced in locating patients in translating their addresses between Chinese and English. It is interesting to note that the follow-up was very much better among women than men. This may be due to the men being more reluctant to ask for time off from work because of fear of losing employment. In the circular letter addressed to all patients an offer was made of financial reimbursement to cover any loss incurred by attending the follow-up clinic.

Each patient at interview was invited to give an account of his progress since operation and his personal impression of the result solicited. A series of leading questions was also asked designed to enquire specifically into symptoms now recognized as being sequelae of ulcer operations. The interview was followed by a clinical examination noting particularly the nutritional state, then the patient's weight and hemoglobin level were recorded. Based on the information obtained a general assessment of each patient's operation result was made and graded as follows: A—symptom-free and no disability; B—mild symptoms not requiring treatment; C—symptoms requiring treatment by conservative measures; D—symptoms causing disability. The information is summarized in Table IV.

As the numbers of patients in the other case groups who attended are too small to be significant, this follow-up report will be confined to the largest group of duodenal ulcer cases for whom vagotomy and pylorectomy were carried out.

Of 92 cases in this group, 70 patients had a result classified as A, 17 as B, 1 as C, and 4 as D. Accepting grades A and B as satisfactory, and grades C and D as unsatisfactory, 87 cases or 94.5 per cent had a satisfactory operative result and 5 cases or 5.5 per cent an unsatisfactory outcome.

Regardless of whether the anastomosis was retrocolic (short loop) or antecolic (long loop) or Billroth I, Table V discloses the analysis of the questionnaire applied to each patient.

Each of these features which were of special interest in assessing the efficacy of vagotomy and pylorectomy will now be commented upon individually.

Bilious vomiting. Frank vomiting of bile indicative of afferent loop stasis was not experienced by any of the patients. However, 15 patients or 17.4 per cent did admit to occasional regurgitation of small amounts of sour tasting fluid into the mouth after meals but in no instance to an extent requiring treatment.

"*Dumping.*" Symptoms that have been attributed to rapid emptying of the gastric

remnant into the efferent loop and labelled collectively the "dumping syndrome" for want of a better term are a well recognized sequel to subtotal gastrectomy in some patients (11.9 per cent of patients of Butler and Capper). They have been variously explained to be due to spasm of the jejunum, distention of the afferent loop, and gravity traction on the gastric remnant, and the symptoms mediated through the autonomic nervous system. In order to elicit the incidence of dumping in our patients, it was enquired of each if they had ever experienced sensations of heat, sweating, faintness, palpitations, or borborygmi after meals since their operation. An unequivocal admission to so doing was given by 1 patient only in this series.

Hypoglycemia. The cause of symptoms of the so called "late postgastrectomy syndrome" are attributable to hypoglycemia and occur 2 to 3 hours after meals. In 2 patients such symptoms occurred and are typified by the account given by 1 of them, who incidentally was the only European in the follow-up series.

CASE REPORT. S. K., aged 52 years, of tall and asthenic build, had a vagotomy and pylorectomy carried out for duodenal ulcer in January 1953. Since then he has been free from pain and in a good general state of health. On rising in the morning he usually feels some nausea, does not feel hungry, and is satisfied to have just tea and toast for breakfast. Lunch is his first main meal of the day which he takes about 1.30 p.m. One and a half to 2 hours later, at the end of the afternoon, he frequently experiences a series of symptoms which he describes as dizziness, a feeling that he is going to "black out," slight nausea, pressure on the forehead, shortness of breath, and as the attack is passing off a slight trembling of the hands and marked perspiration, the whole sequence lasting for 20 to 30 minutes. He had found out quite independently that sweet coffee, tea and biscuits, beef tea, and whisky and ginger ale all cut short the attacks, which first started to occur 8 months after his operation.

A glucose tolerance test showed an oxyhyperglycemic curve and the hypoglycemic nature of his symptoms was confirmed.

He was assured that his symptoms had no serious significance and was advised to continue to abort the attacks in the manner in which he himself had found to be most efficacious, that is, by raising his blood sugar with some rapidly assimilable carbohydrate.

TABLE V.—ANALYSIS OF 92 CASES IN WHICH VAGOTOMY AND PYLORECTOMY WERE PERFORMED FOR DUODENAL ULCER

Postoperative sequelae	*No. of cases*	*Per cent*
Bilious regurgitation	15	16
'Dumping'	1	1
Hypoglycemia	2	2
Cheilosis	12	14
Neuritis	3	3.2
Edema	6	6.5
Rice intake		
Unchanged	60	65.3
Decreased	29	31
Weight		
Maintained or improved	76	82
Decreased	6	6.5
Diarrhea	0	0
Stomal ulceration	0	0

The only case of stomal ulceration was seen in a patient who had vagotomy without complete pylorectomy.

Cheilosis, neuritis, and edema. Evidence of nutritional deficiencies were specifically looked for in respect to angular stomatitis, peripheral neuritis, and edema. Cheilosis was noted in 11 patients or 13 per cent, either alone or in association with a smooth tongue. Mild peripheral neuritis, as manifested by cramps and paresthesias in the limbs with decreased tendon jerks, was recorded in 3 patients or 3.4 per cent and pitting edema of the ankles in 5 or 5.8 per cent. In those patients with pitting edema, in whom the investigation was made, the serum proteins were found to be of normal level and ratio. There was no local cause ascertainable for the edema, and we have presumed its presence to be due to a mild beri-beri state, an extreme example of which came to our notice during the survey. This particular patient was an elderly man for whom a subtotal gastrectomy had been carried out for gastric ulcer 9 months prior to his being seen at the clinic. He was found to be grossly edematous and in incipient cardiac failure. On being investigated in the medical ward a diagnosis of beri-beri was made and a dramatic response obtained to the intravenous administration of thiamine within a few days.

Anemia. Among 79 patients in whom both preoperative and postoperative hemoglobin figures were available only 7 showed a fall in

hemoglobin concentration averaging 1.9 grams, the remaining 72 showing a rise over preoperative figures averaging 3.2 grams. Among these 79 patients, before operation 35 had hemoglobin levels below 11 grams whereas at the time of follow-up only 9 were below this level and, of these, 4 showed a substantial rise over their preoperative level. These figures are of considerable interest when compared with those by Welbourn and his associates who report that after subtotal gastrectomy 20 per cent of men and 30 per cent of women were anemic. In view of the fact that in most of our cases blood was not available in sufficient quantity to do more than replace the loss at operation, it is suggested that the limited resection practiced does not interfere to any significant extent with iron absorption and metabolism, and that consequently after the removal of the source of hemorrhage the body is able to correct a pre-existing anemia.

Rice intake. The amount of rice that could be taken at each meal was unchanged following operation in 56 patients or 67.5 per cent, whereas 27 patients or 32.5 per cent found that their preoperative capacity had been reduced by the operation and were obliged to take smaller meals more frequently as a consequence. Postprandial fullness was, however, admitted by nearly all the patients whether their rice intake had been reduced or not.

Weight. Of those patients for whom a preoperative weight record was available 70 or 92.1 per cent had maintained or improved their weight since operation while 6 or 7.9 per cent had lost weight. Unfortunately few of the patients had any knowledge of what their "health weight" had been in the past; and, therefore, a comparison could only be made objectively with the weight recorded on their admission to hospital prior to operation.

Diarrhea. Diarrhea has been a troublesome disadvantage of vagotomy when carried out alone for peptic ulcer, as reported by several observers. Considering that the vagi provide motor innervation to the intestine the logical expectation would be that vagal section would result in retarded motility of the gut rather than the reverse as in patients experiencing diarrhea. The probable explanation of this paradox is that gastric stasis produced by vagotomy unaccompanied by an adequate drainage procedure allows fermentation of food to occur in the stomach which process is aided by the reduced acidity. The sour gastric contents on entering the small bowel irritate the gut and stimulate it to rapid emptying. This notion is in accord with our experience of vagotomy, when gastric drainage is well provided for via the gastrojejunostomy stoma, as none of the patients in the series were troubled with diarrhea with the exception of 1 patient whose frequent stools were the outcome of short-circuiting too much small bowel in treating a postoperative obstruction.

Mortality. Four deaths were encountered in the series out of 189 patients operated upon, an overall mortality rate of 2.1 per cent. Three of these deaths were due to peritonitis following leakage from the duodenal stump and the other patient died, also of peritonitis, shortly after operative relief of intestinal obstruction that had developed during convalescence from vagotomy and pylorectomy.

COMMENT

In drawing conclusions from this survey we hold the view that the patients who attended for interview are representative of the group of operation cases as a whole. Whether or not such an opinion is justified is open to conjecture but we believe it better to accept the limitations inherent in maintaining contact with patients in Hong Kong over a period of time rather than to ignore the usefulness of such information as can be gained from those who find it possible to attend for examination.

On this basis, vagotomy with pylorectomy appears to be worthy of a place in the treatment of duodenal ulceration. The operative

mortality in the series is similar and no greater than that reported by several authorities for subtotal gastrectomy (3.7 per cent by Visick, 5.7 per cent by Lake, 2 per cent by Wells and Brewer), with which it has in common the greatest technical hazard of the operation, the closure of the duodenal stump.

Relief from the original ulcer symptoms has been achieved in all cases and although it is too early to assume that the dangers of recurrent ulceration, either at the original site or at the stoma, is past, so far we have not encountered any instance of this complication following the completed operation. The persistence of free acid in the fractional test meal in a small proportion of patients although not yet accompanied by stomal ulceration may lead us in the future to practice vagotomy with hemigastrectomy as recommended by Wells, rather than the distal third gastrectomy practiced at present, if in fact stomal ulceration should ever become a problem.

It is gratifying to note that nutritional defects have not been conspicuous. Failure to maintain weight which occurred in 6 patients or 6.5 per cent compares favorably with Muir's 40.7 per cent after subtotal gastrectomy. A factor that has probably helped in this respect is that the majority of the patients are Cantonese of spare build who do not tend to "run to fat" as so many Western patients do on a prolonged ulcer diet before their operation.

The low incidence of vitamin deficiency, the absence of diarrhea, and the improvement in the blood picture serves to indicate that vagotomy with pylorectomy does not lead to intestinal hurry or interfere with food absorption to any significant degree. We believe that the large gastric remnant materially contributes to the maintained nutritional status of these patients. While emptying from the remaining stomach is no longer controlled by a sphincter mechanism, nevertheless, space is provided at the entrance to the intestinal tract for admixture of the food bolus with secretions and adjustment of its osmotic tension before it is received by the small bowel. The rapid precipitation of ingested material into the efferent loop from the small remnant of a subtotal gastrectomy has been invoked as the cause of many of the untoward sequelae of that operation by exciting the bowel to hypermotility consequent upon either unaccustomed distention or spasm provoked by the high undiluted osmotic tension of the inadequately admixed (conditioned) gut contents. Under these circumstances, rapid emptying of the small bowel leads to impaired absorption and resultant malnutrition. If this appraisal is correct, then we should expect to find that the relative absence of nutritional defects after vagotomy and pylorectomy are paralleled by a similar low incidence of the early postgastrectomy syndrome, and this has in fact been our experience as far as the cases that have been reviewed are concerned.

In as much as this survey was carried out as a timely enquiry into the position of vagotomy and pylorectomy, we find that the results are sufficiently encouraging for us to continue its application to the surgical treatment of duodenal ulcer in this area.

SUMMARY

1. The problem of the management of peptic ulceration in Hong Kong is discussed.

2. The desirability of retaining the reservoir functon of the stomach in people eating a bulky diet is stressed.

3. A report of a follow-up survey of 92 patients who had had vagotomy and pylorectomy (⅓ gastrectomy) for duodenal ulcer is given. This number constituted 48.6 per cent of the patients operated upon during the 3 year period from 1952 to 1954.

4. An overall mortality of 2.1 per cent in 189 patients is recorded, and the low incidence of nutirtional defects and mechanical sequelae following operation in the patients who attended for follow-up is noted.

5. It is concluded that the postoperative results of vagotomy and pylorectomy are sufficiently encouraging to warrant the continuance of the operation as the surgical treat-

ment of choice in the management of duodenal ulceration.

REFERENCES

1. Aird, I., Bentall, H. H., Mehigen, J. A., and Roberts, J. A. F. The blood groups in relation to peptic ulceration and carcinoma of colon, rectum, breast, and bronchus; an association between the ABO groups and peptic ulceration. Brit. M. J., 1954, 2: 315.
2. Butler, T. J., and Capper, W. M. Experimental study of 79 cases showing early post-gastrectomy syndrome. Brit. M. J., 1951, 1: 1177.
3. Capper, W. M., and Butler, T. J. Clinical study of post gastrectomy syndrome. Brit. M. J., 1951, 2: 265.
4. Johnson, H. D. Techniques in British Surgery. Edited by Rodney Maingot. Philadelphia and London: W. B. Saunders Co., 1950.
5. Idem. Vagotomy in treatment of peptic ulcer. Ann. R. Coll. Surgeons England, 1951, 8: 160.
6. Johnson, H. D., and Orr, I. M. Surgical policy for peptic ulcer. Lancet, Lond., 1953, 1: 253.
7. Idem. Selective surgery for peptic ulcer. Surg. Gyn. Obst., 1954, 98: 425.
8. Lake, N. C. Aftermath of gastrectomy. Brit. M. J., 1948, 1: 285.
9. Turner, F. P. Acute perforations of stomach, duodenum, and jejunum; an analysis of 224 cases with late follow-up data reported on 147 cases of acute perforated peptic ulcer. Surg. Gyn. Obst., 1951, 92: 281.
10. Visick, A. H. Measured radical gastrectomy; review of 505 operations for peptic ulcer. Lancet, Lond., 1948, 1: 505.
11. Welbourn, R., Hughes, R., and Wells, C. Vitamin-B deficiencies after gastric operations. Lancet, Lond., 1951, 1: 939.
12. Wells, C. A report on the late complications of gastrectomy. Ann. R. Coll. Surgeons England, 1955, 16: 145.
13. Wells, C., and Brewer, A. C. Surgery of duodenal ulcer. Brit. J. Surg., 1947, 35: 364.

EDITORIALS

MINOR OPEN WOUNDS

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ALTHOUGH IN RECENT YEARS serious efforts have been made to educate both the medical profession and the public in regard to the early management of major trauma, too little emphasis has been placed upon the potential dangers of minor injuries. Whereas the borderline between a major and a minor injury is not defined clearly in all instances, it too often is determined by the uninformed on the basis of the obvious visible trauma. The force of the blow, the size of the external wound, or even the initial extent of tissue damage does not always determine the true extent or seriousness of injury. A tiny puncture wound with a long instrument may cause fatal hemorrhage, a superficial abrasion may terminate in fatal infection, and even a simple laceration, if neglected, may result in the loss of a digit or a limb.

Not always can the blame for the unfortunate outcome following minor injury be placed upon neglect on the part of the layman. Too often it must be attributed to lack of judgment on the part of the physician who conducted the original examination and treatment. Most major injuries, because they are disabling from their instigation, are treated early, whereas, those that appear minor, because they seem trivial or because they are not initially painful and disabling, may be neglected or come to treatment late. It is important, therefore, that not only the medical profession but all laymen should recognize the potential danger of minor injuries and that the public should be taught to seek early medical attention. Steps in this direction have been taken in industry and have paid generous dividends, but little has been done to educate the public at home, where most injuries occur.

The most important complicating feature of a minor open wound is infection, but still it is rare that one encounters a layman who has the slightest conception of how or why infection occurs. The inclination of almost anyone who cuts his finger is to place it in his mouth, wrap it with an unsterile handkerchief, and later dab it with merthiolate, iodine, or some other antiseptic solution or salve. Burns and superficial lacerations usually are smeared with butter or a handy ointment and covered with unsterile dressings. These wounds first of all become contaminated with a variety of organisms and then are sealed and contaminated further by the application of an unsterile dressing and, finally, the already damaged tissues are devitalized further by the local application of a caustic agent. How could one better ensure a poor prognosis and what have we, as a profession, done to prevent these unhealthy practices? Almost every first-aid kit to be found consists mainly of antiseptic solution and gauze dressings which long since have become unsterile. Might it not be better to provide soap, running water, and a brush and the knowledge of how these best can be used?

The first principle in the management of any open wound is to keep it clean and to

prevent contamination. This can be accomplished best by thorough and lengthy scrubbing with mild soap and water. Thereafter a sterile dressing will protect the wound from further contamination. The importance of immediate and thorough cleansing of a wide area surrounding all open wounds, no matter how small, cannot be overemphasized. This simple procedure will ensure the reduction of infection to a minimum. The local use of antiseptics in a wound should be condemned. Antiseptics sufficiently strong to kill bacteria in all probability will kill tissue locally and thus enhance rather than prevent infection.

Devitalized tissue as well as retained foreign bodies almost invariably lead to secondary infection and suppuration. Only by careful and painstaking mechanical cleansing of a wound can this be prevented. It is essential, therefore, that all contaminated wounds be inspected thoroughly with proper lighting and with sedation or anesthesia when indicated. The judicious use of local or nerve block anesthesia is particularly useful in this regard. With good anesthesia, adequate scrubbing with soap and water to accomplish a complete débridement often can be carried out by the physician or by the patient himself under circumstances in which it otherwise might be neglected to avoid pain.

Thorough débridement of minor wounds should not be avoided simply because they may appear small. The common practice of suturing small wounds without an initial careful preparation and thorough cleansing must be condemned. Too frequently one encounters widespread cellulitis and lymphangitis secondary to minor wounds of the extremities which have been sutured under questionable circumstances.

The principle of secondary suture as applied to major wounds to avoid suppuration is equally important in the management of minor wounds. Grossly contaminated and questionably infected wounds are best left open and sutured secondarily after the danger of infection has passed.

The second important principle in management is rest, complete rest. This is accomplished best by splinting the injured part. Only when it becomes necessary to control pain does the layman put the injured part at rest and seldom does the physician apply a splint until after infection has become apparent and even then too infrequently. Almost invariably the patient with a minor open wound is treated with the local application of an antiseptic dressing until infection is apparent; then he is most likely told to soak the part several times daily in hot water or hot Epsom salts solution. This time-honored remedy long since has outlived its usefulness. Thorough cleansing with soap and water, the application of a sterile dressing and a splint will prevent infection usually, if instituted early, and frequently will control infection once it has started. It is far better for a patient to undergo the inconveniences of a short period of immobilization to prevent infection than the long period which is frequently necessary to control it.

The judicious use of antibiotics to control infection plays an important part in the management of open wounds, but unfortunately they are used too frequently to the exclusion of the more important principles already mentioned. It is unusual indeed that antibiotics alone will control infection in a contaminated wound. Carefully selected antibiotics should be used only as an adjunct to cleansing and rest.

A closed wound presumably is protected from bacterial contamination by the intact integument, but even a microscopic break may serve as a portal of entry for bacteria. Most closed wounds are caused by contusive violence, which may result in unsuspected subcutaneous tissue damage and hematoma. Such devitalized tissue affords a most favorable pablum for the growth of contaminating bacteria. The latter may enter the wound locally or through the bloodstream, so that an apparently intact skin does not protect necessarily against secondary infection. Under these circumstances the use of antibiotics

in conjunction with proper splinting may prevent unwarranted complications.

It is not the purpose of this discussion to list the various types of minor injuries that may occur and the details of their proper treatment, but rather to emphasize the importance of the recognition both by the public and the physician of the potential dangers of so-called minor injuries.

The great majority of minor injuries are represented by contusions, abrasions, lacerations, sprains, and superficial burns, but none of these should be considered minor until a careful inspection has established the true nature and extent of tissue damage. The borderline between a minor injury and a major one cannot be drawn accurately and obviously depends upon a great many factors, only a small number of which can be defined clearly. The important fact to remember is that almost any minor injury may become a major one under circumstances that can and should be recognized and controlled.

The early recognition of the complete extent of a wound, the prevention of infection by thorough cleansing, and the early institution of rest by careful immobilization constitute the general principles of treatment of most minor soft tissue injuries. When properly applied, these principles of treatment will not only bring about early restoration of function, but will prevent untoward complications and prolonged disability.

DISSECTING ANEURYSM OF THE AORTA

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DISSECTING ANEURYSM of the aorta is associated with a grave prognosis, its course being rapidly fatal in over 75 per cent of cases. Heretofore, treatment has been largely symptomatic and entirely unsatisfactory. These challenging features of the condition, along with the gratifying success that has recently been achieved in the surgical attack upon other forms of aortic disease, have stimulated efforts to develop a more effective and satisfactory means of dealing with this problem.

Because of the pathologic nature of the lesion, excisional therapy, which has proved highly effective in sacciform and fusiform aneurysms, is usually not feasible. One reason for this is that dissecting aneurysms are rarely sufficiently localized. Often the lesion involves the entire aorta. Moreover, it usually arises in the upper reaches of the aorta as a transverse tear in the intima and media just above the aortic valves or near the origin of the left subclavian artery, with separation of the intramural layers of the aorta by the forceful stream of blood. This dissection may then progress circumferentially to involve all or a portion of the aorta and distally down to the bifurcation and even lower to invade the femoral arteries.

The extent and course of the disease are variable. Most patients die within a few hours or days following terminal perforation through the outer wall. Occasionally, however, a patient may survive for months or years, if the dissected passage re-enters the true lumen, usually at some point in the abdominal aorta with formation of a "double-barrelled" aorta. This method of nature to promote healing suggested a clue to an effective surgical approach to the problem at hand.

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The rationale of this procedure is thus based upon nature's attempt to deal with the problem by spontaneous re-entry of the dissected passage at some distal point in the aorta with consequent restoration of peripheral circulation and diminution of tension upon the outer wall to prevent its rupture. The resulting formation of a "double-barrelled" aorta from the origin of the dissection to the point of re-entry tends to equalize the pressures in the true and false lumens permitting sufficient time for the development of periaortic fibrous tissue response to strengthen the outer wall and prevent rupture. While these events are relatively uncommon in the natural course of the disease, the fact remains that this occurrence constitutes virtually the only means of recovery. Fortunately, even in the more severe and acute forms of the disease terminal rupture and death may be delayed for hours or days, permitting sufficient time for application of surgical therapy, but the operation should be considered an emergency procedure.

The essential principles underlying the procedure are the same for most cases, but the surgical approach to be employed may have to be modified according to the nature of the lesion. For instance, dissections beginning in the ascending part of the aortic arch should be treated by creation of a re-entry passage into the aortic lumen above with obliteration of the false passage below. This is accomplished by cross clamping the descending thoracic aorta, dividing it completely between clamps, momentarily releasing the distal occluding clamp to permit escape of blood and clots in the false passage, obliterating the false passage below by approximating the outer and inner layers with a continuous suture, excising a small segment from the inner wall above to produce

re-entry of the outer lumen, and then performing end-to-end anastomosis. In this way blood flow from the double aortic lumen above is diverted into the single normal lumen below. Obviously this procedure is not curative since the dissecting aneurysm remains above the point of division of the aorta. Under these circumstances, in which the dissecting process begins in the ascending aorta and invades the entire aortic arch, excisional therapy is not at present considered feasible. Accordingly the operation is directed toward correction of the process by interruption of its progress and creation of conditions compatible with function and eventual repair. The essential objective here is to produce re-entry of the false passage into the normal lumen as close to the point of origin of the dissection as may be feasible for several reasons. By thus shortening the extent of the false passage peripheral resistance to blood flow tends to be reduced, thus diminishing the likelihood of rupture of the weakened outer wall until it can be strengthened by periaortic fibrous tissue response. In addition, restoration of blood flow through the normal aortic lumen in the descending thoracic aorta tends to correct the compressive ischemic effects of the false passage upon the points of origin of the major vascular channels of the abdominal aorta.

If the lesion is fairly well localized and arises at or below the level of the left subclavian artery, a more curative procedure is possible by combining the operation previously described with excisional therapy. This is accomplished by excision of the segment involved in the origin of the dissection, obliteration of the false passage below by suture of the inner and outer wall, and restoration of continuity by insertion of an aortic homograft.

These methods of treatment have been employed in 10 patients, 7 of whom recovered. Two patients died about 1 week after operation from rupture, presumably from uncontrolled hypertension, and the other from ventricular fibrillation, probably resulting from pneumothorax and hypothermia. The results in the 7 successful cases have been most gratifying, with complete relief of symptoms and resumption of normal activity. The first patient who was operated upon 14 months ago has remained well and an aortogram performed 3 months after operation in this case revealed a relatively normal outline of the descending thoracic aorta. Evaluation of this method of operative correction of dissecting aortic aneurysms obviously must await further experience, but the early gratifying results suggest that it offers a more effective approach to the problem than has been heretofore available.

THE SURGEON AT WORK

SURGICAL TECHNIQUE OF LIGATION OF INFERIOR MESENTERIC ARTERY AND PREAORTIC LYMPHADENECTOMY

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LIGATION OF the inferior mesenteric artery and preaortic lymphadenectomy have been carried out in a sufficient number of cases to establish this procedure as relatively safe. If the surgical principles are followed which have been established and accepted for many years in cases of cancer of other areas of the body, as in carcinoma of the breast when the lymphatic structures about the axillary vessels and the chest wall are removed, then preaortic lymphadenectomy should be carried out as a part of the surgical procedure used in the treatment of cancer of the left colon and rectum. Ligation and section of the inferior mesenteric artery at its origin facilitate the preaortic lymphadenectomy and make it more complete. At present, there is still hesitancy in the minds of many to accept this procedure as a truly valid one. The reasons given are: (1) an increase in the total length of the operation; (2) fear for the blood supply to the remaining intestine; (3) if carcinoma is present in the aortic nodes removed, it has spread beyond this point; and last, but not least, (4) the technical difficulty of ascertaining the exact point of origin of the artery on the aorta.

An increase in operating time is no contraindication for the procedure if the possibility of a higher percentage of cures is considered. Of course, prolonging an operation of this kind is still subject to the rational points governing a lengthy procedure in the face of poor risks. The great majority of patients whom we have operated upon do not fall into the category of poor risks.

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That the blood supply to the remaining intestine is adequate in most individuals has been proved clinically in a sufficient number of cases. The report of Shaw and Green is the only one in the literature recording serious consequences (death) following this extended resection. The present series consists of 75 consecutive cases, and in none was any impairment of the blood supply encountered to the colon used in anastomosis or as a colostomy. To avoid the possibility of a gangrenous bowel, it has been made routine to observe the flow of blood coming through the open end of the marginal artery after the inferior mesenteric artery has been divided. The suggestion, presented by Shaw and Green, of occluding the inferior mesenteric artery prior to sectioning, is excellent. In none of the present series of cases was it considered necessary to resect a greater length of bowel than had been anticipated prior to division of the inferior mesenteric artery. Division of the marginal artery causes a sharp delineation between viable and nonviable bowel.

If carcinoma is present in the lymphatics removed by preaortic lymphadenectomy, as in 17 per cent of specimens cleared by Bacon and Trimpi, there is a possibility that further extension has occurred, but there is also the satisfaction of knowing that as much as possible has been done to cure the patient. Certainly, in a small number of these patients, the extended operation will make the difference between a cancer cure and a failure.

It is the purpose of the present article to present our technique of aortic lymphadenectomy and inferior mesenteric artery ligation. The work was begun several years ago by measuring

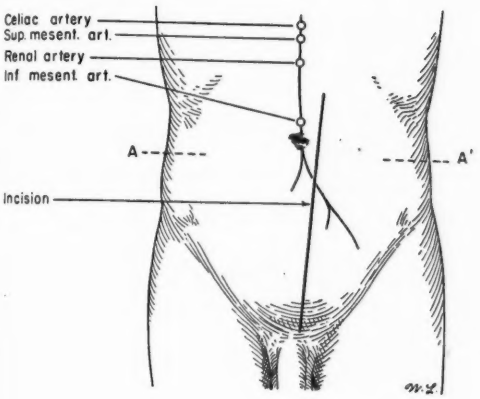

FIG. 1.

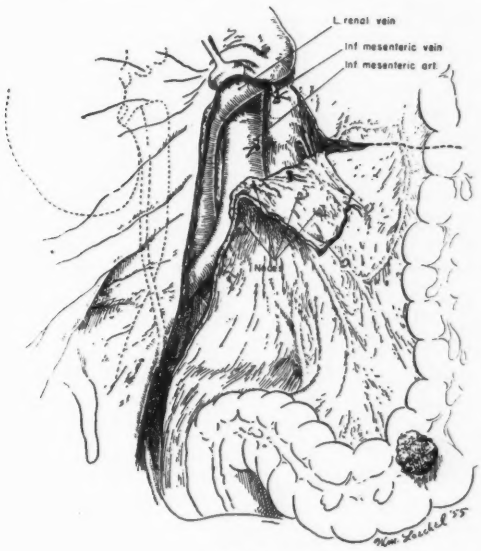

FIG. 3.

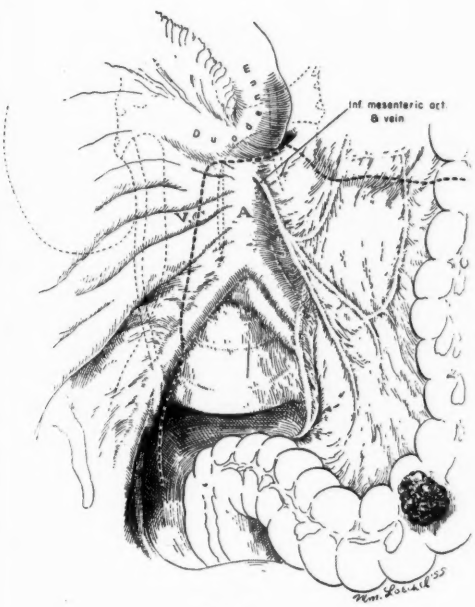

FIG. 2.

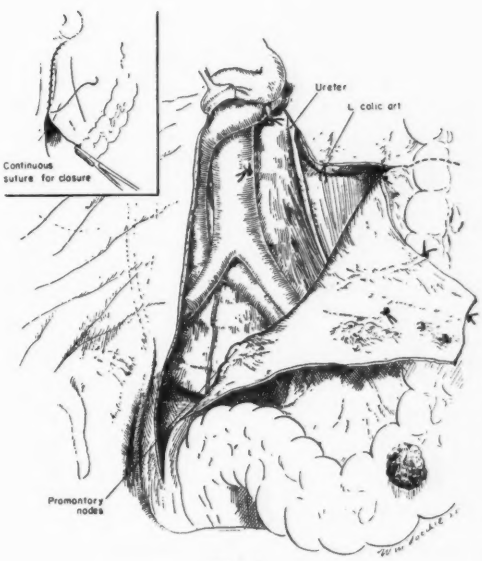

FIG. 4.

FIG. 1. Left lower abdominal incision. Topographic average location of abdominal aortic branches supplying the gastrointestinal tract. (Redrawn from Gray's *Anatomy*, 24th ed., p. 1345.)

FIG. 2. Posterior peritoneal incision represented by dotted line. Dissection begun at lower duodenal border.

FIG. 3. The duodenum has been displaced upward and to the right. The left renal vein comes into view. The inferior mesenteric vein and artery have been ligated.

FIG. 4. Preaortic lymphadenectomy completed from lower border of renal vein to promontory group of nodes. Left colic artery ligated.

the distance between the sacral promontory, the bifurcation of the aorta, and the origin of the inferior mesenteric artery. It was thought that if the exact average location of the artery was known the procedure would be expedited which proved correct as long as the approach to the artery was from the region of the bifurcation of the aorta. Cantor, in a recent monograph, aided in these studies by showing that no correlation exists between sex, age, and size of an adult individual, and the measurements between the promontory of the sacrum, the aortic bifurcation, and the origin of the inferior mesenteric artery. Recently, the surgical approach to this region has been changed and further measurements are no longer necessary.

Prerequisites for performing aortic lymphadenectomy as herein described include an incision long enough for adequate exposure (Fig. 1) and adequate packing off of the small bowel for visualization of the lower border of the duodenum over the inferior vena cava and aorta. After the resectability of a tumor of the sigmoid or rectum has been determined with the lesion disturbed as little as possible, ligatures are placed on the bowel above and below the tumor as suggested by Cole and his associates (4, 5). Dissection is started at the lower border of the duodenum (Fig. 2) which is elevated upward and to the right. The left renal vein is easily located as it crosses the aorta under the upper border of the duodenum. The peritoneal incision is continued down over the aorta and vena cava, then laterally to the inferior mesenteric vein which is ligated at this level, or preferably higher, and as close to the lower border of the pancreas as permitted by this exposure (Fig. 3). The left ureter is identified lateral and posterior to the inferior mesenteric vein. The lymphatic tissue in the anterior and lateral aspects of the aorta and vena cava is then removed in continuity from above downward (Fig. 4). The inferior mesenteric artery is ligated during this procedure. Removal of lymphatic tissue from the lateral pelvic walls and vessels may then be done in continuity with the dissection, if the lesion is one involving the tissues at the level of, or below, the rectal peritoneal reflexion. Otherwise, it the lesion is in the left colon, sigmoid, or intraperitoneal rectum, the lymphatic tissue dissection is completed at the removal of the promontory nodes and fat.

By beginning the dissection away from the cancer and interrupting the routes by which cancer cells may be disseminated (bowel lumen, venous channels, and lymphatic channels), the spread of the cells which may be desquamated or separated from the lesion itself as a result of handling the tumor may be prevented.

CONCLUSION

The surgical technique of preaortic lymphadenectomy and inferior mesenteric arterectomy is described. Some of the pros and cons to this procedure are discussed briefly.

REFERENCES

1. Ault, G. W., Castro, A. F., and Smith, R. S. Clinical study of ligation of inferior mesenteric artery in left colon resections. Surg. Gyn. Obst., 1952, 94: 223.
2. Bacon, H. E. Quoted by Cantor (3).
3. Cantor, M. O. The effect of stature upon the point of origin of the inferior mesenteric artery. Surgery, 1954, 36: 80.
4. Cole, W. H., Packard, D., and Southwick, H. W. Carcinoma of the colon with special reference to prevention of recurrence. J. Am. M. Ass., 1954, 155: 1549.
5. McGrew, E. A., Laws, J. F., and Cole, W. H. Free malignant cells in relation to recurrence of carcinoma of the colon. J. Am. M. Ass., 1954, 154: 1251.
6. Shaw, R. S., and Green, T. H., Jr. Massive mesenteric infarction following inferior mesenteric artery ligation in resection of the colon for carcinoma. N. England J. M., 1953, 248: 890.

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The Book Shelf

JOHN CLARENCE WEBSTER, JOHN MONTGOMERY BALDY, AND THEIR OPERATION FOR UTERINE RETROVERSION

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THE SECOND HALF of the last century ushered in an era that has been characterized as "the dark ages of operative furor" in the treatment of uterine retroversion, then the commonest gynecologic disease. The leading gynecologists of the period regarded retrodisplacement of the uterus as a frequent cause of a large variety of complaints in women. The importance imputed to retroversion is abundantly evident in the textbooks of the day. In the narrative volume *Clinical Notes on Uterine Surgery*, published in 1866, J. Marion Sims tells of a lady who "was riding on a pony in the suburbs of the city of Montgomery, Alabama, where I then resided. It took fright and suddenly jumped from under her—she fell, striking her pelvis on the ground. I saw her soon afterwards; her sufferings were very severe. Besides the contusions from the fall, she complained of rectal and vesical tenesmus. On examination, I found a complete retroversion of the uterus. . ."

Equally impressive is Sir James Young Simpson's introduction to his lecture on retroversion, which appears in his *Clinical Lectures on the Diseases of Women:* ". . . A patient who came to my house the other day remarked that she had come walking, and added that it was the first time she had walked out of doors for 3 years. Such an incident is of not infrequent occurrence. The lady I refer to talked with another, with whose sister she was acquainted, and that sister had for about fifteen years been unable to walk; and I wish to teach you today what it was that prevented these ladies, as it prevents others, from walking, and to teach you also how you may relieve their symptoms and rectify their malady."

Against such a background of authoritative teaching a large number and variety of surgical procedures developed for the cure of retroversion, and the operations were practiced with abandon indeed. "The round ligaments were folded, ligated, plicated, shirred, plaited, planted, transplanted, replanted, drawn over, above, and through the broad ligaments and fastened to the back of the uterus," as stated by Fluhmann. Mr. Alexander of Liverpool, the inventor of a well known and probably the first suspension operation, having been asked by a group of visiting surgeons in 1911 to demonstrate it, stated that he sent 1 of his 4 assistants into the north, 1 into the east, 1 into the west, and 1 into the south of Liverpool but that each returned after diligent search with the report that in all of that great city he had been unable to find one woman who had not already had the Alexander operation for suspension of the uterus.

Suspension operations for the primary purpose of correcting uterine retroposition have fallen greatly in popularity in the past several decades and are now carried out almost exclusively as incidental procedures in conjunction with myomectomy, tubal plastic operation, and the conservative surgical therapy of pelvic inflammatory

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disease and endometriosis. Among the best known of the suspension procedures developed in America, and still performed occasionally today, is the Baldy-Webster operation.

The operation consists of drawing a limb or knuckle of each round ligament behind the uterus through a perforation made in the broad ligament, and suturing the round ligaments posterior to the corpus, thereby supporting the latter in an anterior position. This principle was probably carried out in 1900 or earlier by a Dr. Andrews of Chicago, according to Baldy (4), but the first description of the operation was published in 1901 by Webster. This report was a model of brevity, the entire text and an illustration comprising but 1 column of 1 page in the *Journal of the American Medical Association* (Fig. 1).

John Clarence Webster was born in Shediac, New Brunswick, Canada, October 21, 1863 and died there on March 16, 1950. He studied medicine at Edinburgh, where he won the gold medal for his thesis, first prize for research in 1894 and 1896, and a total of 14 prizes and awards between the years 1883, when he received his degree of doctor of medicine, and 1896, when he returned to Canada to become associated with McGill University and the Royal Victoria Hospital. For 6 years following his graduation at Edinburgh he worked as assistant to Sir Alexander Simpson, Professor of Midwifery. In 1899, Webster was called to Chicago to the chair of obstetrics and gynecology at Rush Medical College, where he remained until 1919, when he returned to his native Canada because of poor health. While in Chicago the Websters began a collection of oriental objets d'art, which subsequently became one of the most famous in the world, containing an outstanding section of Japanese prints. After returning to Shediac, Webster developed a deep interest in Canadian history and devoted himself to its study and to the collection of historical mementos. The Webster Collection of Canadiana was the second largest in existence when donated to the New Brunswick Museum. Webster was responsible for establishing a number of historical museums and the restoration of several others. In recognition of this interest he was appointed to the Historic Sites and Monuments Board of Canada and served for a period as Chairman. His withdrawal from practice proved far from a retirement.

Baldy's association with the Baldy-Webster operation appears to be based upon the vigor of his writings and his bold personality rather than upon his contribution to the development of the operation itself. His first description of his suspension operation, in which the round ligaments were divided, differed significantly from the procedure described earlier by Webster:

"The following operation," wrote Baldy (1) in 1902, "which I have devised after much thinking and experimenting, retains every advantage of [Webster's] operation and does away with all its disadvantages.

"The round ligament on each side of the uterus is picked up and a ligature thrown about it close to the uterus, so placed as to secure the artery. The round ligaments are then severed close to the ligatures. This leaves the uterine ends of the ligaments ligated and the other ends free and bleeding. The bleeding is controlled by a fine ligature to each vessel or by sutures which fasten them in the next step of the operation. A pair of forceps is now made to perforate the broad ligament from its posterior aspect (at the point at which the round ligament is cut on the anterior surface), and the cut end (the pelvic end) of the round ligament is grasped in the bite of the forceps . . . and pulled through the hole in the broad ligament (made by the forceps in perforating) until it protrudes on the posterior side of the broad ligament. The opposite side is treated in a similar manner. The cut ends of the round ligaments are now attached by means of sutures to the cornua of the uterus directly back of the original point of attachment of the normally attached round ligament. . . The point of attachment may be higher or lower than this, as the surgeon may find necessary to accomplish the result. If necessary as much of the round ligament is cut off, before suturing it to the uterus, as is necessary to take up any slack and give the proper amount of tension and support to the uterus. This ends the operation. The suture is a continuous one and may be either chromicized gut or silk. The effect of this procedure is to draw the fundus of the uterus upward and forward into a perfect position."

Baldy later modified his technique (2, 3), so that the operation ultimately became almost identical to the procedure originally devised by Webster, but nowhere in Baldy's writings is any indication to be found of modesty toward his own work or of diplomacy in his expressed views of the work of others. The opening paragraph of his 1902 paper reads:

"Alexander's operation is of course a thing of the past except in the hands of a few—a very few. It will die altogether, like all transitional operations, in the future. Hysterorrhaphy, ventrosuspension, or whatever else one cares to call this class of operations, will most probably follow in its footsteps shortly."

In his later evaluation of the operation (2, 3), Baldy wrote: "I have performed it almost constantly . . . modifying it here and there at times as apparent difficulties arose and as it seemed necessary to overcome certain objections and certain faults in results; and I find at the present time a completed technic which is, I think, perfect."

"The one point in the operation . . ." he stated in 1915 (4), "which I hold superior to all other operations is the fact that when the operation is performed not only is the uterus itself put in a proper position but the ovaries are also replaced and held up at a proper level without any extra manipulation. I do not hold that this is done better than in any other operation because there is no other operation in which it is done at all. . ."

Overlooked by subsequent generations of gynecologists, but far greater to his credit than the operation with which his name is associated, is the dissenting voice raised by John Baldy in protest against the promiscuous practice of uterine suspension. As early as 1909 he wrote: "Retrodisplacements of the uterus are mostly coincidental with other lesions, and where such is the case the symptoms almost universally come from the associated disease. . . 'The treatment of retrodisplacements' is then a misnomer; it should be 'the treatment of conditions in connection with which retrodisplacements of the uterus occur as an incident.'"

Baldy's fearless remarks at a symposium on the surgical treatment of retroversion of the uterus, sponsored by the Philadelphia Medical Society, December 9, 1914, may not have endeared him to his colleagues but left no doubt as to his feelings. The other members of the symposium included John G. Clarke, Howard A. Kelly, Barton Cooke Hirst, Edwin B. Cragin, J. Wesley Bovée, D. Tod Gilliam, J. Clarence Webster, and E. E. Montgomery. Baldy, the concluding speaker, stated:

". . . I am not at all sure that I am justified in taking part in a meeting of this character holding the views I do on the subject. In my opinion

RETROVERSION OF THE UTERUS. 913

A SATISFACTORY OPERATION FOR CERTAIN CASES OF RETROVERSION OF THE UTERUS.

J. CLARENCE WEBSTER, M.D.

Professor of Obstetrics and Gynecology, Rush Medical College, Affiliated with the University of Chicago; Obstetrician and Gynecologist, Presbyterian Hospital.

CHICAGO.

During the past year I have carried out the following procedure in a number of cases where operative interference has been deemed advisable for retroversion of the uterus.

The patient being in the Trendelenburg position, the abdomen is opened, adhesions are separated and other pathologic conditions, which may be present, attended to. The fundus of the uterus is elevated and pushed forward. A small hole is then made through the broad ligament on one side under the utero-ovarian ligament near the uterus. Through it a pair of forceps is passed from behind in order to grasp the round ligament about an inch from its uterine end. The latter is then pulled through the broad ligament in a double fold. It is carried across the back of the uterus a short distance above the utero-sacral ligaments and is then stitched in this

Diagram representing the round ligaments doubled up, drawn through the broad ligaments and stitched to the posterior surface of the uterus above the utero-sacral ligaments.

position with chromic catgut. A similar procedure is carried out on the other side, the second round ligament being stitched to the back of the uterus above or below the first one or crossing it. The amount of overlapping of the round ligaments depends upon their length and laxity.

Each ligament is also stitched to the edge of the hole in the broad ligament. As a result of this operation, the round ligaments are much shortened and through their new attachment to the posterior and lower part of the uterus, act both in elevating the uterus as a whole and in preventing it from returning to its retroverted position. The ovaries are also elevated. No raw surface is produced on which adhesions can form. No new ligamen' is formed to act as a possible cause of intestinal obstruction and of trouble in pregnancy and labor. The normal range of uterine movements is not materially altered. There is no possibility of any interference with pregnancy and labor.

The operation can be performed equally well by vaginal section. It seems, therefore, to me to be more advantageous than the other operative procedures commonly employed in the treatment of retroversion of the uterus.

FIG. 1. Webster's original paper on the surgical treatment of uterine retroversion. (From the *Journal of the American Medical Association*, 1901, 37: 913.)

nine-tenths of the operations performed on women for retrodisplacements are uncalled for. . .

"As to the number of operations performed for this condition under any circumstances, Dr. Cragin is such an old and warm friend that I would hate to tell him what I thought of him for doing two hundred retrodisplacement operations in a single year. In order not to be too personal to Dr. Cragin I would like to include in that remark all the speakers of the evening who are sitting on the platform with me.

". . . it looks to me as though the possible number of retrodisplacement operations performed in this country is limited only by the number of females in existence."

John Montgomery Baldy was born in Danville, Pennsylvania, on June 16, 1860. He studied medicine at the University of Pennsylvania, graduating in 1884, and after an internship at the Philadelphia Hospital, engaged in general practice in Scranton for a few years. He then returned to Philadelphia for special study in gynecology and in 1891 was appointed Professor of Gynecology at the Old Philadelphia Polyclinic Hospital, later becoming surgeon in chief at the Gynecean Hospital. He was one of the first advocates of the radical surgical treatment of pelvic inflammatory disease. His most important literary product was *The American Textbook of Gynecology*, which he edited. In 1908 he served as President of the American Gynecological Society.

Baldy was greatly interested in raising the standards of medical training, and was appointed in 1912 as President of the Pennsylvania Bureau of Medical Education and Licensure. He inaugurated the State's requirement of a year's internship for eligibility for medical licensure examination and established minimum standards for all hospitals employing interns. He later served as the State Commissioner of Welfare for 2 years, before his retirement in 1923. He died at his home in Devon on December 12, 1934.

REFERENCES

1. Baldy, J. M. A new operation for retrodisplacement. Am. J. Obst., 1902, 45: 650–654.
2. Idem. Treatment of uterine retrodisplacements. Surg. Gyn. Obst., 1909, 8: 421–434.
3. Idem. Operation for retrodisplacement of the uterus. J. Am. M. Ass., 1911, 56: 481–484.
4. Idem. The surgical treatment of retroversion of the uterus. Surg. Gyn. Obst., 1915, 20: 614–615.
5. Clarke, J. G. The operative treatment of retroversion of the uterus. Surg. Gyn. Obst., 1915, 20: 597–598.
6. Davis, C. H. John Clarence Webster, 1863–1950. Gyn. Trans., 1950, 73: 263–265.
7. Fluhmann, C. F. The rise and fall of suspension operations for uterine retrodisplacement. Bull. Johns Hopkins Hosp., 1955, 96: 59–70.
8. Heaney, N. S. John Clarence Webster, 1863–1950. Proc. Inst. M. Chicago, 1950, 18: 174–176.
9. Priest, F. O. Dr. John Clarence Webster. Canad. M. Ass. J., 1951, 64: 351–353.
10. Schumann, E. A. John Montgomery Baldy, 1860–1934. Gyn. Trans., 1935, 60: 339–342.
11. Simpson, J. Y. Clinical Lectures on the Diseases of Women. P. 764. Edinburgh: Adam and Charles Black, 1872.
12. Sims, J. M. Clinical Notes on Uterine Surgery. P. 15. New York: William Wood & Co., 1866.
13. Webster, J. C. A satisfactory operation for certain cases of retroversion of the uterus. J. Am. M. Ass., 1901, 37: 913.

Reviews of New Books

THE AUTHORS have analyzed 298 cases of histologically proved gliomas seen at the St. George's Hospital during a 10 year period from August 1937 to August 1947 in the volume *Intracranial Gliomata*.[1] The analysis is detailed, descriptive, and concise. It considers almost every conceivable aspect and is well described by text and numerous charts. The cases are studied and analyzed from four main aspects. The first is that of the patient's characteristics, including sex and age, as related to onset, duration of illness, and tumor type. The second considers tumor characteristics with regard to pathology, location, duration, and prognosis. The third describes the symptoms, both primary and secondary, and their relation to the patient and tumor characteristics. The fourth aspect is that of treatment, including surgery and radiology with results and prognosis. The statistical findings of the analysis are tabulated from every possible angle. The 69 pages represent a timely, valuable, and perhaps the most detailed report available. It is excellent for statistical reference and is highly recommended as important and informative reading to all interested in the subject. —*David Cleveland.*

THE VOLUME entitled *Clinical Orthopaedics*[2] has been published twice a year and the present book represents the fifth edition since its inception. The symposium of this volume is on backache. The material by the individual contributors is better organized than previously and duplication is kept to a minimum. One hopes these qualities will be continued in future volumes.

Subject matter covers the postural evolution, examination, conservative treatment, manipulative and surgical treatment of low back pain, with chapters on the cervical and the dorsal spine.

The second section on general orthopaedics has useful clinical material and some stimulating theoretical material. —*Kenath H. Sponsel.*

IN THE FOREWORD of the book *Salivary Gland Tumors*[3] by Donald E. Ross, the author delineates beautifully the problems and confusion attending the management of salivary gland tumors. However, this book does little to clarify these problems in the mind of this reviewer.

The diversity of opinion among contemporary pathologists as to the classification of these tumors seems to handicap a truly definitive presentation of the subject, since each surgeon must lean heavily upon his personal pathologist in determining what is, or is not, cancer. This along with the capricious clinical behavior of salivary gland tumors, the necessity of an exceptionally long follow-up and the relatively small number of some lesions observed during an average surgical practice makes for difficulty in fitting the treatment to the pathology. The author attempts to by-pass uncertainty of pathologic diagnosis by relying upon one type of operation.

Under the classification of Benign Neoplasms the shading of malignancy which has confused so many observers is emphasized and the author in describing mixed tumors under the benign division makes the statement, "Those who have had the most experience with these tumors now regard them as malignant."

Cylindromata (adenocarcinoma, cylindroma type) are included under benign tumors in the classification. Excerpts from the literature presented under this heading predominantly support the view that these tumors are decidedly malignant, yet the author takes no stand except to classify them as benign.

Under Malignant Tumors the author makes the statement, "All recurrent tumors should be regarded as malignant, at least locally so." Later he says "More and more we are regarding all tumors as being malignant and we remove the whole gland more and more frequently."

The author repeatedly condemns biopsies. He believes that needle biopsies are inadequate, frozen section biopsies rarely helpful, and biopsies as a whole "meddlesome surgery." His objections are that biopsy tends to spread tumor cells and that, "the tumor must be removed adequately in any case." It is believed that his criticism of *improperly* performed biopsy and *tumor spillage* is justified, but that most surgeons would regard his stand as being too dogmatic and the performance of incisional biopsy with proper safeguards as being necessary in some instances.

The author's fundamental idea is the gospel of facial nerve preservation, and this book repeatedly and forcefully impresses on the reader that tumors of the parotid gland may be removed adequately without fragmentation and without facial nerve paralysis.

Criticism could be leveled at his handling of malignant tumors and the statement, "It may be seen, therefore, that it is possible to do the most radical operations and yet save the nerves," is inaccurate. In his zeal to prevent facial paralysis the author does not mention that an expanding tumor, benign or malignant, pushes the facial nerve before it and becomes so closely approximated that it is necessary to dissect the nerve from the tumor surface if it is to be preserved. Regardless of the amount of gland tissue removed a block removal has not been accomplished and the dissection has gone much too close to the tumor in the event of malignancy.

The author's personal cases are presented in Chapter 4. The experience with parotid gland malignant tumors is limited to 13 cases, 3 of which are described as border line.

[1] INTRACRANIAL GLIOMATA; SOME CLINICAL, RADIOLOGICAL AND THERAPEUTIC ASPECTS OF 298 CASES. By John Penman and Marion C. Smith. Medical Research Council Special Report Series, No. 284. 70 pages. $.90. London: Her Majesty's Stationery Office, 1954.

[2] CLINICAL ORTHOPAEDICS. By Anthony F. DePalma, Editor-in-Chief. With the assistance of the Associate Editors and the Board of Advisory Editors. No. 5. 242 pages, illustrated. $7.50. Philadelphia and Montreal: J. B. Lippincott Co., 1955.

[3] SALIVARY GLAND TUMORS. By Donald E. Ross, M.D., F.A.C.S., F.I.C.S., F.R.C.S. (Eng.), F.R.C.S. (Edin.). 86 pages, illustrated. $7.50. Springfield, Ill.: Charles C Thomas, 1955.

All except 1 patient who died following surgery had postoperative radiation. In only 1 case did the author believe that it was necessary to sacrifice the entire facial nerve.

Of neck dissections, he says "Where definite malignancy is present in the gland, we now do a block dissection of the neck." The type of neck dissection is not discussed, nor is "definite malignancy" defined.

Experienced surgeons dealing with cancer within the parotid gland have seen parotid malignancies that invade facial nerve, bone, and other adjacent structures. While trying to evaluate each case on its merit and to avoid needless paralysis it would seem that often the principles of good cancer surgery would demand a more complete procedure than that indicated by the author as being typical.

Surgical anatomy is presented well.

The author's technique of parotidectomy is described in detail and illustrated by artists' drawings. The procedure is somewhat oversimplified since each operation may present different problems depending on the size, position, and character of the tumor.

Other related conditions of the parotid gland are mentioned but not described in detail. The history of the subject and the histogenesis of parotid tumors are outlined. The book deals principally with the parotid gland. A large bibliography is included.

The strength of this book lies in the author's conviction of the inherent threat of a parotid tumor, his insistence upon the principle of total removal without fragmentation, and his confidence in anatomy and technique to safeguard the face from paralysis.

Its weakness is a failure to face the challenge of basic pathology and the realization that there are worse fates than a facial paralysis. —*Louis Byars.*

IT IS DIFFICULT not to speak in extravagant terms of these well written, beautifully illustrated volumes entitled *A History of Medicine*[4] which Dr. Major has written and illustrated with so many striking photographs, a considerable number taken by himself. This work is more than a history of medicine, it brings to the reader a comprehensive outlook on the history of mankind, seen particularly from the standpoint of man's efforts to learn the secrets of the human body, of life itself, and of the conquest of disease.

In his preface Dr. Major says, "This book is . . . written primarily for the medical student and the medical practitioner, in an attempt to interest them more in the history of their own profession, which, despite attacks and abuse, despite quacks and charlatans, and in spite of its own mistakes, has proved itself more enduring than any of the civilizations which gave birth to it." No student or practitioner in reading these volumes can fail to feel a thrill of new pride in his profession and in the realization that he is a member of a great and distinguished company.

In Volume I, Major follows the history of medicine from the "dawn" to the seventeenth century. The first 100 pages, "The Dawn of Medicine," could well serve as an extensive review of what in high school days we termed Ancient History. The Mayas, Aztecs, Incas, and Peruvians, the Babylonians and Assyrians, the Egyptians and East Indians, Hebrew and Chinese medicine, Imhotep, "the first figure of a physician to stand out clearly from the mists of antiquity" (Osler), Susruta, Charaka, and Hua T'o, "the greatest Chinese surgeon of antiquity," come to life in these pages and bring to the reader a feeling of understanding of ancient lore and a sense of keen enjoyment.

There follow sections on Greek and Roman medicine, medicine in the Roman Empire, and, in the remainder of Volume I, sections on the Middle Ages, the Renaissance, and the Seventeenth Century.

In Volume II, devoted to the history of the development of medicine during and after the eighteenth century, there is a very skillful blending of the story of medical progress as it developed in different countries and different centers—Holland, Great Britain, France, Germany, America, Edinburgh, Vienna, and the development of the allied sciences in their relation to medicine—physiology, chemistry, pathology, bacteriology, and radiology. Great names follow one another in rapid succession, and almost without exception there are admirable portraits and other illustrations to add interest and verisimilitude.

At the end of each section are "biographical addenda," arranged alphabetically, with brief notes of men of note who are not included in the more detailed account of the nation or school or group discussed in the section itself.

It would be unnecessary, and perhaps a little presumptuous, to attempt a more detailed review of this interesting work. The reader will have the joy of discovering for himself the physical appearance of men whose names he has heard so often, and of learning something of their character and personality, of their antecedents, of the hardships and handicaps they suffered, of the advantages they enjoyed, and of their contribution to medical progress.

When medical men are asked what a grateful patient might give them as a gesture of appreciation, or what a son or daughter might give as a birthday reminder they could not do better than to ask for this *History of Medicine.* —*Sumner L. Koch.*

A MANUAL on the methods of study currently employed by a number of investigators in the field of blood coagulation is the volume entitled *The Coagulation of Blood.*[5] Its purpose is to make available techniques for the study of various aspects of blood coagulation to investigators and technicians in this field. These techniques, in many instances, are described by investigators who originally employed them. Each contribution has been carefully outlined and edited. The object of the method and the principle involved are clearly stated when possible. The reagents, steps, and procedure are described in detail and the precautions and sources of error for the particular test are also described.

This monograph should serve as a very useful aid to investigators and technicians in the field of blood coagulation and will be of particular interest to any newcomer to the field. It is not intended as a reference

[4] A HISTORY OF MEDICINE. By Ralph H. Major, M.D. Vols. I and II. 1155 pages, illustrated. $14.50. Springfield, Ill.: Charles C Thomas. 1954.

[5] THE COAGULATION OF BLOOD; METHODS OF STUDY. Edited by Leandro M. Tocantins, M.D. 240 pages, illustrated. $5.75. New York and London: Grune & Stratton, 1955.

but rather as a working laboratory manual. It serves its purpose admirably. —*J. Garrott Allen.*

BRITISH OBSTETRICIANS and gynecologists have always been major contributors to the evolution of clinical obstetrics and gynecology. A new work, *British Obstetric and Gynecological Practice*,[6] edited by Sir Eardley Holland and Aleck Bourne, is, therefore, of more than passing interest because it presents a cross section of present day British teaching and techniques. The editors have arranged the material in 2 volumes; one on obstetrics edited by Holland, the other on gynecology edited by Bourne. The 64 chapters contained in the 2 volumes were written by 46 contributing authors from many of the British teaching centers.

The overall approach to both subjects is directed toward their clinical aspects. Emphasis is placed on practical matters in a manner which should make the work of interest and value to students and general practitioners as well as to those who have had specialized training. Consideration of the basic sciences is limited to acquainting the reader with essential fundamentals. New discoveries and theoretic or disputative matters are either omitted or briefly mentioned. The dynamic and beautifully written chapter on "Cesarean Section" by the late McIntosh Marshall and the well arranged and informative one on "Fertility, Infertility, and Sterility" by John Stallworthy merit special mention. They are like brisk draughts blowing through the pleasing but quiet air of conservatism and formality which characterizes the tenor of both volumes.

In the obstetric volume a consideration of normal pregnancy, labor, and the puerperium is followed by chapters devoted to "Diseases Associated with Pregnancy," difficult labor, obstetric complications, and operative obstetrics. The chapters on "The Psychosomatic Approach to Childbirth" by Grantley Read, "Psychiatry and Obstetrics" by G. W. B. James, and the discussion of the medicolegal aspects of obstetrics by a barrister-of-law, John B. Gardner, are welcome additions to the literature. For the most part, the teaching principles are very similar to those found in American textbooks. American readers will be interested in the emphasis placed upon the management of home deliveries, the use of the flying obstetric squad, and transportation of the patient to the hospital.

The gynecologic text begins with chapters on "The Reproductive Cycle," embryology of the genitalia, examination of the patient, "Disorders of Menstruation," and "Puberty and the Menopause." These are followed by a consideration of the disorders of each genital organ. The last portion of the book consists of chapters devoted to infections, endometriosis, prolapse, fistulas, and infertility. The 2 final chapters on "The Psychiatry of Gynecology" and the "Medico-Legal Aspects of Gynecology" are of unusual interest and outstanding merit. In this volume, as in the one on obstetrics, the general tone is one of conservatism. Typical clinical pictures, accepted diagnostic techniques and approved methods of treatment are presented in a well organized and rather formal fashion. The most critical reader will have difficulty restraining his admiration for the very excellent chapter on "The Cervix Uteri" by J. B. Blaikley. It is lucidly written, gives a brief but good review of normal anatomy and histology, a clear exposition of many cervical diseases, and is beautifully illustrated. The part devoted to radiation therapy of cervical carcinoma warrants particular commendation. In many of the chapters normal histology and histopathology could have been given more place and the rationale of treatment dealt with in more detail.

The editors and their talented corps of associates, in their presentation of *British Obstetric and Gynecological Practice*, have created a work which covers both fields in a sound, conservative, and useful manner.

—*John W. Huffman.*

IN THE THIRD EDITION of *Intestinal Obstructions*[7] Wangensteen has drawn from a rich background of clinical experience to produce a scholarly work on this fascinating field of surgery. In the 13 year period since the publication of the second edition, the author has added greatly to his own material and there have been important changes in the techniques and even the instruments used in bowel obstruction surgery. All of these changes are thoroughly covered.

The book is excellently balanced in content and arrangement of material. The first chapter is a detailed consideration of the effects of distention and contains much experimental work on the physiologic disturbances wrought by obstruction, much of which work was done by the author himself. The bibliography at the end of this chapter is quite detailed; like that at the end of each chapter it covers the older and more recent literature on the topic equally well.

Succeeding chapters in this 26 chapter work are logically arranged in sections devoted to diagnosis, therapeutic considerations, including operation, and special types of obstruction. The work is enhanced by pithy case reports totally contained in the captions beneath illustrations of the pertinent roentgenograms and operative specimens. The illustrations are of good quality; the numerous tables are well done and quite illuminating, especially those on mortality rates. Comment on the make-up of the book would not be complete without specific mention of the fine author index and the almost total absence of typographic errors.

The author's sound surgical philosophy is well elucidated. It is particularly helpful in its delineation of the operative attack and the conservative approach, emphasizing the criteria used to determine which method should be employed. An occasional gem of personal philosophy is phrased in first-person narration by the author and gives the book a warm flavor, much as if the reader had Wangensteen standing at his elbow counseling him. In this regard there is a

[6] BRITISH OBSTETRIC AND GYNECOLOGICAL PRACTICE. Edited by Sir Eardley Holland, M.D. (Lond.), F.R.C.P., F.R.C.S., F.R.C.O.G., and Aleck Bourne, M.A., M.B., B.Ch. (Cantab.), F.R.C.S., F.R.C.O.G. A two volume set. Obstetrics. By Sir Eardley Holland. Gynecology. By Aleck Bourne. 2022 pages, 767 illustrations. $29.50. Philadelphia: F. A. Davis Co., 1955.

[7] INTESTINAL OBSTRUCTIONS; PHYSIOLOGICAL, PATHOLOGICAL, AND CLINICAL CONSIDERATIONS WITH EMPHASIS ON THERAPY, INCLUDING DESCRIPTION OF OPERATIVE PROCEDURES. By Owen H. Wangensteen, B.A., M.D., Ph.D. 3rd ed. 838 pages, 200 illustrations. $15.50. Springfield, Ill.: Charles C Thomas, 1955.

good discussion of the "second look" operation and summation of the author's experience with it. A strong plea is made for the use of aseptic, or closed type, anastomoses throughout the gastrointestinal tract. Many other specific features of the book should be mentioned, among them the detailed analysis of electrolyte requirements of patients with bowel obstruction, the whole chapters devoted to operative procedures, the discussion of acute abdominal injuries, and the short but informative reports of other surgeons' experiences in radical removal of great lengths of gangrenous small bowel.

This is an excellent book on intestinal obstructions, truly a reference work. It should be read by every surgeon who works in this field.

—*Benjamin F. Lounsbury.*

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

CLINICAL ORTHOPAEDICS. Anthony F. DePalma, Editor-in-Chief. With the assistance of the Associate Editors, the Board of Advisory Editors, and the Board of Corresponding Editors. Number 6. 219 pages, illustrated. $7.50. Philadelphia and Montreal: J. B. Lippincott Co., 1955.

TRAITÉ DE TECHNIQUE CHIRURGICALE. By B. Fey, P. Mocquot, S. Oberlin, J. Quénu, P. Truffert, M. David, M. Iselin, R. Dossot, R. Dubau, Ch. Dubost, J.-J. Galey, Y. Longuet, J. Loygue, J. Mathey, F. Palmer, J. Perrotin, J. Rudler, G. Thormeret, and J. Varangot. 2nd rev. ed., Vol. IV. 1330 pages, 864 illustrations. 8800 fr. Paris: Masson & Co., 1955.

L'INCONTINENZA URINARIA NELL'UOMO E NELLA DONNA E SUO TRATTAMENTO. By Bruno Geremia and Antonio Tormene. With a preface by Prof. G. Ceccarelli. 278 pages, 70 illustrations. Bologna: Cappelli Editore, 1955.

A ENDOSCOPIA ABDÔMINO-PELVIANA EM GINECOLOGIA. By Paulo Gorga. 280 pages, 84 illustrations. São Paulo, 1954.

THE BILIARY TRACT; WITH SPECIAL REFERENCE TO THE COMMON BILE DUCT. By Julian A. Sterling, A.B., M.D., M.Med.Sc., Sc.D., F.A.C.S. 424 pages, 94 illustrations. $10.00. Baltimore: The Williams & Wilkins Co., 1955.

CITODIAGNOSTICA IN CONTRASTO DI FASE DEL CARCINOMA DELL'APPARATO GENITALE MULIEBRE. By Dott. Massimo Macciotta and Dott. Alfonso Bertaglia. 215 pages, 170 illustrations. Bologna: L. Cappelli, Editore, 1955.

LEHRBUCH DER GEBURTSHILFE. By Prof. Dr. Heinrich Martius. With the assistance of Prof. Dr. Werner Bickenbach and Käthe Droysen. 3rd rev. ed. 757 pages, 777 illustrations. $14.25. Stuttgart: Georg Thieme Verlag, 1956.

HYPNOSIS AND ITS THERAPEUTIC APPLICATIONS. Edited by Roy M. Dorcus, Ph.D. 327 pages. $7.50. New York, Toronto, London: McGraw-Hill Book Co., Inc., The Blakiston Division, 1956.

ARTHROPLASTY. By St. J. D. Buxton, M.B., B.S., F.R.C.S. 126 pages, 43 illustrations. $6.00. Philadelphia and Montreal: J. B. Lippincott Co., 1955.

ARCHIVIO "PUTTI" DI CHIRURGIA DEGLI ORGANI DI MOVIMENTO. Directed by O. Scaglietti. Edited by L. Gui. Vol. V. 599 pages text, 170 pages, bibliography, illustrated. Firenze: Edizioni Scientifiche dell'—Istituto Ortopedico Toscano, 1954.

I TUMORI PRIMITIVI DELLO SPAZIO RETROPERITONEALE. By Vittorio Pettinari. Relazione tenuta al LVII Congresso della Società Italiana di Chirurgia, Roma, 3-6 ottobre 1955. 283 pages, 29 illustrations. Roma: Edizioni Mediche e Scientifiche, 1955.

CHEST X-RAY DIAGNOSIS. By Max Ritvo, M.D. 2nd ed., thoroughly rev. 640 pages, 633 illustrations on 426 figures and 1 color plate. $16.00. Philadelphia: Lea & Febiger, 1956.

SURGERY IN WORLD WAR II. VASCULAR SURGERY. Edited by Daniel C. Elkin, M.D., and Michael E. DeBakey, M.D., Medical Department, United States Army. 465 pages, 56 illustrations. Washington, D.C.: Office of the Surgeon General, Department of the Army, 1955.

FORMEN DES POSTTRAUMATISCHEN KOPFSCHMERZES (DER NEURALGISCHE SCHMERZ). By Dr. Elmar E. Bues. With a foreword by Prof. Dr. R. Wanke. 111 pages, 23 illustrations. DM 9.60, $2.35. Stuttgart: Georg Thieme Verlag, 1956.

CONGENITAL HEART DISEASE. Report of the Fourteenth M & R Pediatric Research Conference. 118 pages, 28 illustrations. Issued by M & R Laboratories, Columbus 16, Ohio.

POSTURAL BACK PAIN. By Milton C. Cobey, M.D., F.A.C.S. 78 pages, illustrated. $3.00. Springfield, Ill.: Charles C Thomas, 1955.

THE BLOOD-BRAIN BARRIER; WITH SPECIAL REGARD TO THE USE OF RADIOACTIVE ISOTOPES. By Louis Bakay, M.D., F.A.C.S. 154 pages, 32 illustrations. $5.50. Springfield, Ill.: Charles C Thomas, 1956.

CANCER OF THE LUNG; PATHOLOGY, DIAGNOSIS, AND TREATMENT. By Milton B. Rosenblatt, M.D., and James R. Lisa, M.D. 330 pages, illustrated. $15.00. New York: Oxford University Press, 1956.

THE DIABETIC'S COOKBOOK. By Clarice B. Strachan. 304 pages. $6.50. Houston: The Medical Arts Publishing Foundation, 1955.

INTEGRATED GYNECOLOGY: PRINCIPLES AND PRACTICE. Vols. I, II, and III. By I. C. Rubin, M.D., and Josef Novak, M.D. 1767 pages text, 102 pages index, and 508 illustrations. $60.00. New York, Toronto, London: McGraw-Hill Book Company, Inc., The Blakiston Division, 1956.

A. M. A. SCIENTIFIC EXHIBITS 1955. Sponsored by Council on Scientific Assembly, American Medical Association. 784 pages, illustrated. $20.00. New York: Grune & Stratton, 1955.

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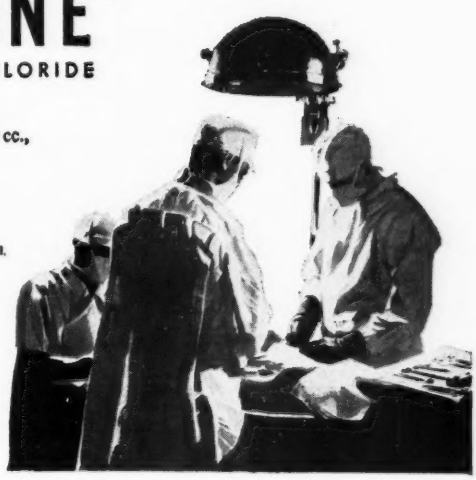

References:

1. Bonica, J. J.: *Anesthesiology*, 11:716, Nov., 1950.
2. Moore, D. C.: *J. A. M. A.*, 146:803, June 30, 1951.
3. Bonica, J. J.: *Anesth. & Analg.*, 30:76, Mar.-Apr., 1951.
4. Bonica, J.J.: The Management of Pain. Philadelphia, Lea & Febiger, Sept., 1953.
5. Moore, D.C.: Regional Block. Springfield, Ill., Charles C. Thomas, 1953.

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